RECORD OF MEDICINE

GENERAL PRACTICE CLINICS

VOL. 166 NO. 6 JUNE 1953

INTERNATIONAL RECORD OF MEDICINE

THE EXPERIMENTAL AND CLINICAL EVALUATION OF l-ARTERENOL, A HORMONE OF THE ADRENAL MEDULLA — *Maurice L. Tainter*

ENDOCRINES AND PSYCHIATRY — *Francis J. Braceland*

PAN AMERICAN MEDICAL WOMAN'S SECTION

TERRAMYCIN THERAPY IN BURNS — *H. D. Ritchie and A. B. Wallace*

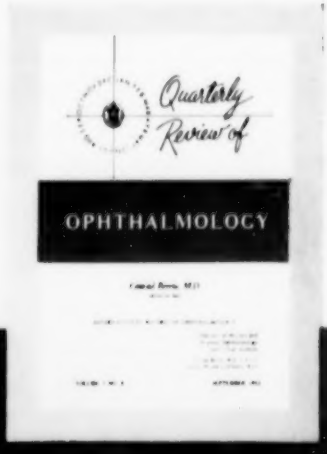
GENERAL PRACTICE CLINICS

Each month a major medical specialty is featured.

in this issue

QUARTERLY REVIEW OF OPHTHALMOLOGY

Conrad Berens, M.D.
Editor-in-chief



Instant Relief from Headaches!

Does a patient ever berate you because his flat top bifocals cost more than a friend was charged elsewhere for "identical" lenses?

The catch, of course, is in "identical." And it's true—so many bifocals, good and bad, look so much alike that a patient may wonder.

But not when you prescribe K Ultex. There's no mistaking a K. K is the one and only flat top onepiece bifocal. Identification is easy and positive.

K has no imitators. There are no "just as good" competitors. The man who wears K's knows what he has, and can see that the lenses which cost less are not the same. He's satisfied. You're never on the spot. So banish your "competitive brand" headaches. Prescribe K Ultex.

Continental

INDIANAPOLIS

International
RECORD OF MEDICINE
A Journal of Advanced Experimental and Clinical Reports
and
GENERAL PRACTICE CLINICS

ORIGINALLY PUBLISHED AS AMERICAN MEDICAL INTELLIGENCER, FOUNDED PHILADELPHIA, 1837

VOL. 166 NO. 6 • WHOLE NUMBER 2844 • JUNE 1953

Published Monthly by

MD PUBLICATIONS, Inc.

910 17th St., N.W., Washington, D.C.

Editorial Office
30 East 60th Street
New York 22, N. Y.

Circulation Offices
910 17th S.T., N.W.
Washington, D. C.
and
30 East 60th Street
New York 22, N. Y.

Advertising Department
30 East 60th Street
New York 22, N. Y.

A cumulative cross reference index is included in the final issue of each volume. Subscription rate: 1 year, $11 00; 3 years, $28.00. Copyright 1953 by MD Publications, Inc. Entered as second class matter at Washington, D. C. under the Act of March 3, 1879. Printed in U. S. A.

COLPOTABS™

THERAPEUTIC VAGINAL INSERT TABLETS · pH 4

NEW SPECIFIC TRICHOMONACIDE

- Unsurpassed Trichomonacide
- Clears Leukorrhea
- Eliminates Vaginal Malodor
- Relieves Pruritus
- Restores Vaginal Acid pH Physiologically
- Increases Tissue Resistance

tyrothricin	2.0 mg.
chlorophyllin	10.0 mg.
beta lactose	1170.0 mg.
phenylmercuric acetate	0.75 mg.
sodium lauryl sulfate	7.5 mg.

PF SINCE 1892

The Purdue Frederick Company

PHARMACEUTICALS FOR THE MEDICAL PROFESSION · NEW YORK 14

EDITORIAL BOARD

FELIX MARTI IBAÑEZ, M. D., *International Editor*

National

FRED L. ADAIR, M.D., *University of Chicago*
HARRY L. ARNOLD, JR., M.D., *Editor, Hawaii Medical Journal, Honolulu, Hawaii*
W. WAYNE BABCOCK, M.D., *Temple University*
HOWARD C. BALLENGER, M.D., *Northwestern University*
CONRAD BERENS, M.D., *The Ophthalmological Foundation*
ALEXANDER W. BLAIN, M.D., *Wayne University*
ALFRED BLALOCK, M.D., *Johns Hopkins University*
W. F. BRAASCH, M.D., *Mayo Clinic*
J. MACKENZIE BROWN, M.D., *University of Southern California*
MORTON S. BRYER, M.D., *The Mount Sinai Hospital*
LEROY A. CALKINS, M.D., *University of Kansas*
BAYARD CARTER, M.D., *Duke University*
RUSSEL L. CECIL, M.D., *Cornell University*
CO TUI, M.D., *Creedmoor Institute*
GEORGE MORRIS COATES, M.D., *University of Pennsylvania*
WILLARD R. COOKE, M.D., *University of Texas*
FREDERICK A. COLLER M. D., *University of Michigan*
WALTER T. DANNREUTHER, M.D., *New York University*
CLYDE L. DEMING, M.D., *Yale University School of Medicine*
R. S. DINSMORE, M.D., *Cleveland Clinic*
HENRY DOLGER, M.D., *New York, N. Y.*
I. E. DRABKIN, PHD., *The College of the City of New York*
DANIEL C. ELKIN, M.D., *Emory University*
LUDWIG A. EMGE, M.D., *Stanford University*
HAROLD K. FABER, M.D., *Stanford University Hospital*
HARRY A. FELDMAN, M.D., *State University of New York*
JOSEPH H. FOBES, M.D., *New York Medical College*
A. STONE FREEDBERG, M. D., *Harvard Medical School, Boston, Mass.*
WILLIS D. GATCH, M.D., *University of Indiana*
LOUIS J. GELBER, M.D., *Rockville Center, L. I., N. Y.*
N. C. GILBERT, M.D., *Northwestern University*
DAVID GROB, M.D., *Johns Hopkins Medical School*
BERNARD J. HANLEY, M.D., *University of Southern California*
FRENCH K. HANSEL, M.D., *Washington University*
CLYDE A. HEATLY, M.D., *University of Rochester*
HENRY F. HELMHOLTZ, M.D., *Mayo Clinic*
FRANK HINMAN, M.D., *University of California*
PAUL H. HOLINGER, M.D., *University of Illinois*
CLARENCE B. INGRAHAM, M.D., *University of Colorado*
CHEVALIER L. JACKSON, M.D., *Temple University*
J. BAY JACOBS, M.D., *Georgetown University*
MARVIN F. JONES, M.D., *New York, N. Y.*
ROBERT W. KEETON, M.D., *University of Illinois*
HARRY H. KERR, M.D., *George Washington University*
WILLIAM J. KERR, M.D., *Blue Lake, California*
I. NEWTON KUGELMASS, M.D., *New York, N. Y.*
CARL H. LENHART, M.D., *Western Reserve University*
THEODORE LIDZ, M.D., *Yale University School of Medicine*
DEAN M. LIERLE, M.D., *University of Iowa*
RALPH H. MAJOR, M.D., *University of Kansas*
IRVINE MCQUARRIE, M.D., *University of Minnesota*
CHARLES M. NORRIS, M. D., *Temple University*
ALTON OCHSNER, M.D., *Tulane University*
THOMAS G. ORR, M.D., *University of Kansas*
HENRY BOYLAN ORTON, M.D., *New York Polyclinic*
WINFRED OVERHOLSER, M.D., *George Washington University*
JAMES E. PAULLIN, M.D., *Emory University*
FRANKLIN L. PAYNE, M.D., *University of Pennsylvania*
LOUIS E. PHANEUF, M.D., *Tufts College Med. School*
E. D. PLASS, M.D., *University of Iowa*
TRACY J. PUTNAM, *Beverly Hills, California*
FRED W. RANKIN, M.D., *Lexington, Kentucky*
B. O. RAULSTON, M.D., *University of Southern California*
LYMAN G. RICHARDS, M.D., *Harvard University*
LEONARD G. ROWNTREE, M.D., *Miami, Fla.*
RAYMOND SACKLER, M.D., *New York N. Y*

Milton S. Sacks, M.D., *University of Maryland School of Medicine*

Morris Schaeffer, M.D., *Director, Communicable Disease Center, Montgomery, Ala.*

Lewis C. Scheffey, M.D., *Jefferson Medical College*

Sidney Schiellis, M.D., *University of Maryland School of Medicine*

Edward A. Schumann, M.D., *Philadelphia, Pa.*

Cyrus C. Sturgis, M.D., *University of Michigan*

Herbert Thoms, M.D., *Yale University*

Donald V. Trueblood, M.D., *Seattle, Wash.*

Norris W. Vaux, M.D., *Jefferson Medical College*

Theodore E. Walsh, M.D., *Washington University*

James J. Waring, M.D., *University of Colorado*

Karl M. Wilson, M.D., *University of Rochester*

Fred W. Wittich, M.D., *Minneapolis, Minn.*

EDITORIAL BOARD

International

Roma Amyot, M.D., *Editor-in-Chief, L'Union Medicale du Canada*

Gaston Bachelard, M.D., *Directeur de l'Institut d'Histoire des Sciences, La Sorbonne, Paris, France*

Paul Diepgen, M.D., *Director of Medizinhistorischen Institutes der Johannes Gutenberg Univ., Mainz, Germany*

Pedro Lain Entralgo, M.D., *President of the Universidad de Madrid, Madrid, Spain*

Prof. A. Gigon, *Schweizerische Akademie der Medizinischen, Wissenschaften, Basel, Switzerland*

Edv. Gotfredsen, M.D., *Director of the Universitetets Medicinsk-Historiske Museum, Copenhagen, Denmark*

Douglas Guthrie, M.D., *Professor of the History of Medicine, University of Edinburgh, Edinburgh, Scotland*

Willy Hartner, M.D., *Johann Wolfgang Goethe Universität, Frankfurt a. M., Germany*

E. Hintzche, M.D., *Anatomisches Institut, Bern, Switzerland*

Juan B. Lastres, M.D., *Profesor de Historia de la Medicina, Universidad de San Marcos, Lima, Peru*

Adolf Meyer-Abich, M.D. *Hamburg-Blankenese, Elbchaussee 460, Germany*

Anibal Ruiz Moreno, M.D., *Profesor de Historia de la Medicina, Buenos Aires, Argentina*

Prof. Rodolfo Pérez de los Reyes, *Universidad de La Habana, Cuba*

Augusto Pi-Suñer, M.D., *Instituto de Fisiologia Experimental, Caracas, Venezuela*

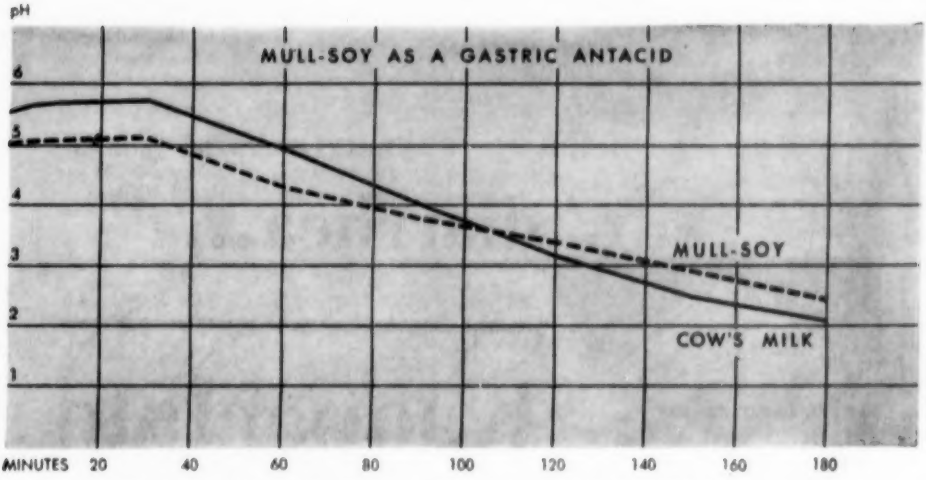
Ilse Rosenthal-Schneider, M.D., *The University of Sydney, Sydney, Australia*

Kenneth F. Russell, M.S., F.R.A.C.S., *Associate Professor of Anatomy, The University of Melbourne, Melbourne, Australia*

Th. H. Schlichting, M.D., *Amsterdam, Holland*

Prof. Ivolino da Vasconcellos, *President, Sociedad Brasileña de Historia da Medicina, Rio de Janeiro, Brazil*

THE USE OF MULL-SOY® IN THE ULCER DIET



We believe that physicians treating ulcer patients will be interested in MULL-SOY for their dietary management. This soybean food, although originally designed for patients who are allergic to milk, exhibits the following important features for all ulcer diets:

1. MULL-SOY exhibits an acid buffer curve which is equal to or better than that which is found with cow's milk.
2. MULL-SOY forms NO curds with digestive enzymes and forms only very finely divided curd particles under the influence of gastric acid.
3. The fat content of MULL-SOY is high in glycerides of the unsaturated fatty acids, especially linoleic.
4. MULL-SOY contains a significantly higher amount of lecithin (a fat emulsifying phospholipid) as compared to the negligible amount in cow's milk.

Professional samples of MULL-SOY are available to physicians who are interested in undertaking trial dietary regimes for gastric ulcer patients.

Write for a supply to Dept. JF.
PRESCRIPTION PRODUCTS DIVISION
The Borden Company · 350 Madison Avenue, New York 17

Upjohn

diarrhea...

Kaopectate

Trademark Reg. U. S. Pat. Off.

Each fluidounce contains:

Kaolin . . . . . 90 grs.

Pectin . . . . . 2 grs.

in an aromatized and carminative vehicle

Available in bottles of 10 oz. and 1 gallon

The Upjohn Company, Kalamazoo, Michigan

INTERNATIONAL RECORD OF MEDICINE

and

GENERAL PRACTICE CLINICS

VOL. 166 NO. 6 • WHOLE NUMBER 2811 • JUNE 1953

INTERNATIONAL RECORD OF MEDICINE

The Experimental and Clinical Evaluation of l-Arterenol, A Hormone of the Adrenal Medulla ... 227
Maurice L. Tainter

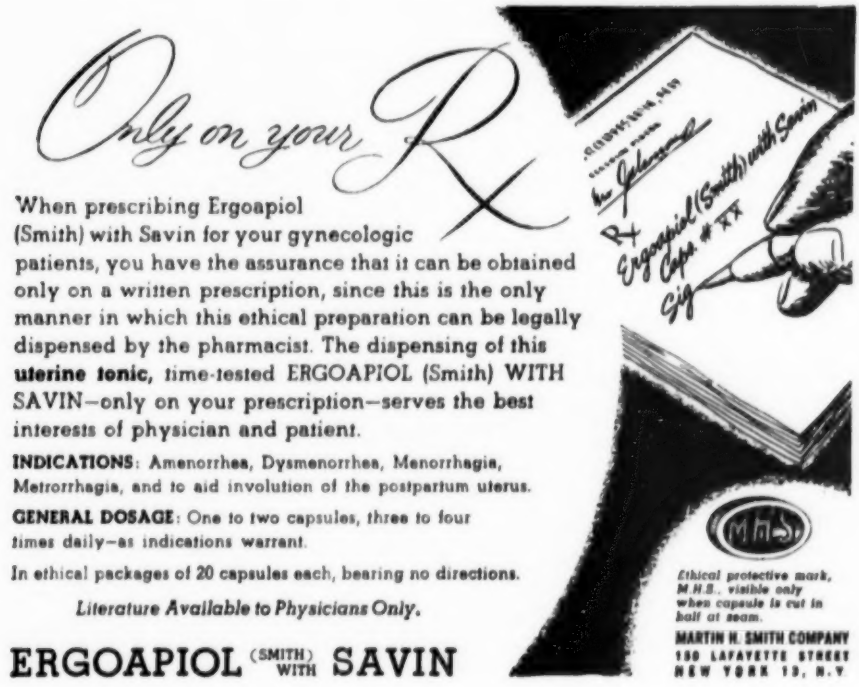
Endocrines and Psychiatry ... 236
Francis J. Braceland

Medical Woman's Section

Terramycin Therapy in Burns ... 241

GENERAL PRACTICE CLINICS

The Use of Myanesin (Tolserol) in Black Widow Spider Bite ... 246
A Complicated Case of Primary Hyperthyroidism ... 246
Varicella Pneumonia ... 246



When prescribing Ergoapiol (Smith) with Savin for your gynecologic patients, you have the assurance that it can be obtained only on a written prescription, since this is the only manner in which this ethical preparation can be legally dispensed by the pharmacist. The dispensing of this **uterine tonic,** time-tested ERGOAPIOL (Smith) WITH SAVIN—only on your prescription—serves the best interests of physician and patient.

INDICATIONS: Amenorrhea, Dysmenorrhea, Menorrhagia, Metrorrhagia, and to aid involution of the postpartum uterus.

GENERAL DOSAGE: One to two capsules, three to four times daily—as indications warrant.

In ethical packages of 20 capsules each, bearing no directions.

Literature Available to Physicians Only.

Ethical protective mark, M.H.S., visible only when capsule is cut in half at seam.

ERGOAPIOL (SMITH) WITH SAVIN

MARTIN H. SMITH COMPANY
150 LAFAYETTE STREET
NEW YORK 13, N.Y.

Quarterly Review of **OPHTHALMOLOGY**

Incorporating the International Record of Ophthalmology

OPHTHALMOLOGY ABSTRACTS

Optics, Physiology and Psychology of Vision
Maximum Electrical Response of the Human Retina on Stimulation with Monochromatic Light of Various Wave Lengths 251
Luminance Thresholds for the Resolution of Visual Detail During Dark Adaptation 251

Diagnostic Methods of Examination, Biomicroscopy and Photography
Some Contributions to the Clinical Application of Electroretinography 252
Memory Aid for the Parallax Test 252
The Truth About "False" Torsion 252

Ocular Movements and Motor Anomalies, Nystagmus, Reading Disability
The Two Phases of Abnormal Retinal Correspondence 253

Anomalies of Refraction and Accommodation, Contact Lenses
How a Correcting Lens Changes the Length of the Eye 253
Effect of Accommodation on the Retinal Image 254
Lens Replacement of Accommodative Activity 254
Clinical Observations in Myopia and Techniques for Myopia Control 254

Cornea, Sclera and Tenon's Capsule
Changes in Corneal Tissue during Conservation and Their Probable Effect on the Postoperative Course of Corneal Transplantation 255

Anterior Chamber and Pupil
Iridectomy for Drawn-up Pupil 255

Uveal Tract and Sympathetic Ophthalmitis
The Vogt-Koyanagi Syndrome 255
Multiple Malignant Melanomas in One Eye 256

Crystalline Lens
Modern Trends in Cataract Surgery 256

Retina
The Early Physical Signs in the Retina Seen in Essential Hypertension 257

Neuro-Ophthalmology, Optic Nerve, Visual Pathways, Centers and Visual Fields
Infectious Mononucleosis with Diffuse Involvement of the Nervous System 258
Traumatic Cranial Injuries. Neurosurgical Diagnosis and Treatment 258
The Optic Chiasm 259
Visual Field Studies in Neurosurgical Problems 259

Eyeballs, Exophthalmos and Enophthalmos
Evisceration with Plastic Intrascleral Implants 261

Glaucoma and Hypotony
Aqueous Outflow Measurements by Continuous Tonometry in Some Unusual Forms of Glaucoma 262
Clinical Studies on Glaucoma 262

Orbit
Carcinoma of the Orbit and Adnexa 263

Anesthesia
Akinesia of the Orbicularis 264

Medical Ophthalmology
New Air Force Visual and Ophthalmological Requirements 264

Comparative Ophthalmology
Otrivin in Ophthalmology 265
Antihistaminic Drugs in Dermatology 265

Miscellaneous
On the Comparative Use of Silver Nitrate and Penicillin in the Eyes of the Newborn 266

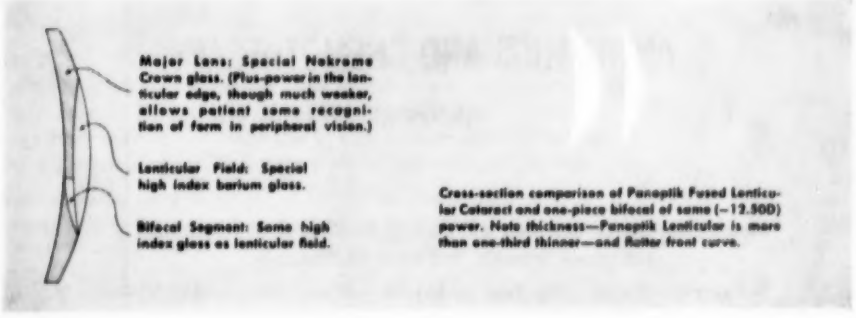
. . . the Cataract Bifocal . . . as good to look at . . . as it is good to look through

BAUSCH & LOMB

Fused Lenticular Panoptik

Optical performance and cosmetic appearance are mutual considerations to the practitioner who seeks to give satisfaction and peace-of-mind to the post-operative cataract patient. From both standpoints, the Panoptik Lenticular Cataract bifocal provides a new standard of excellence. Lighter in weight, thinner in construction and with front curves resembling normal prescriptions, this design is greatly superior in appearance to earlier cataract lenses. Optically, it offers a wide reading field at normal reading level. Great flexibility is afforded in placement of optical centers. Flexibility, too, in base curves—bi-convex, plano base or −3.00 base—can be produced from the same blank. This facilitates service from the laboratory—a single pair of blanks, in each of the called-for reading additions, constitutes a stock from which any aphakic prescription can be made.

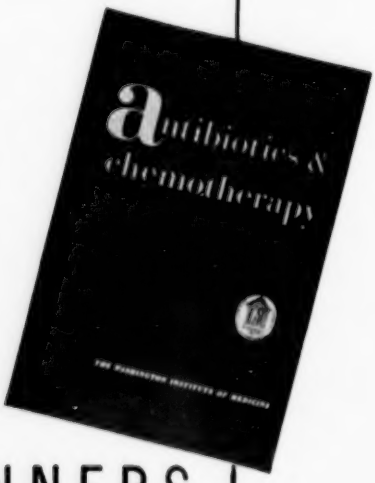
In Soft-Lite, too


Major Lens: Special Nokrome Crown glass. (Plus-power in the lenticular edge, though much weaker, allows patient some recognition of form in peripheral vision.)
Lenticular Field: Special high index barium glass.
Bifocal Segment: Same high index glass as lenticular field.
Cross-section comparison of Panoptik Fused Lenticular Cataract and one-piece bifocal of same (−12.50D) power. Note thickness—Panoptik Lenticular is more than one-third thinner—and flatter front curve.

1853/1953 INTO A NEW CENTURY OF OPTICAL PROGRESS

BAUSCH & LOMB CENTENNIAL

6



NOBEL PRIZE WINNERS

E. CHAIN
SIR ALEXANDER FLEMING
SIR HOWARD W. FLOREY
BERNARDO A. HOUSSAY
E. C. KENDALL
SELMAN A. WAKSMAN

AMONG THE 75 DISTINGUISHED MEMBERS ON THE EDITORIAL BOARD OF ANTIBIOTICS AND CHEMOTHERAPY

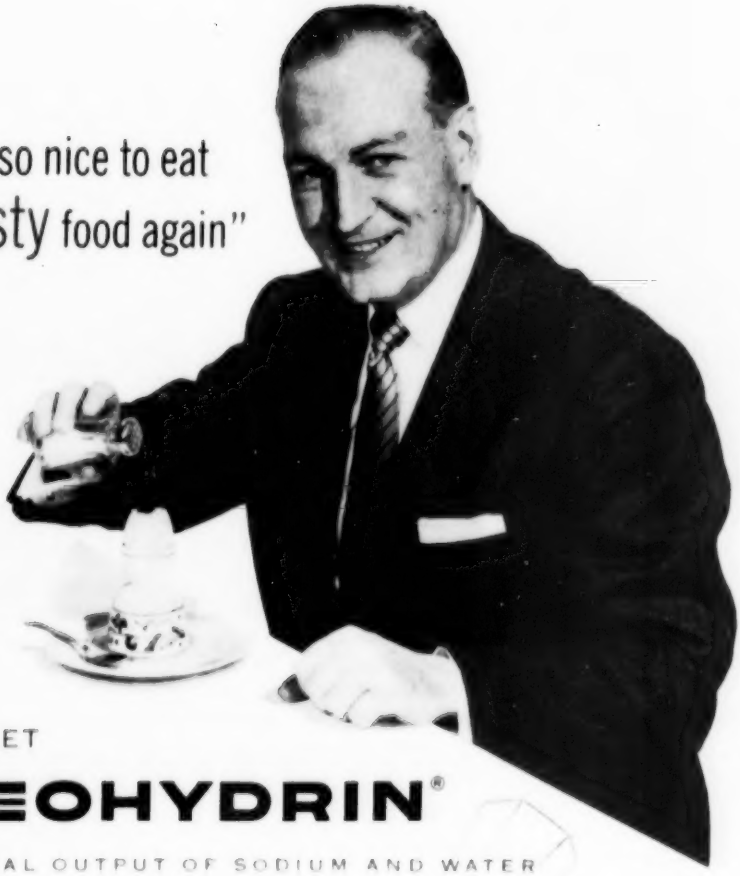
HENRY WELCH, Editor-in-Chief

Monthly Reports on Research and Clinical Application of Antibiotics, Hormones, Steroids, and other Biochemicals

Subscription Rates: One Year — $11.00 — Three Years — $28.00

Published Monthly by the WASHINGTON INSTITUTE OF MEDICINE

Editorial Offices: 30 East 60th Street, New York 22, N. Y.



TABLET

NEOHYDRIN®

NORMAL OUTPUT OF SODIUM AND WATER

PRESCRIBE NEOHYDRIN whenever there is retention of sodium and water except in acute nephritis and in intractable oliguric states. You can balance the output of salt and water against a more physiologic intake by individualizing dosage. From one to six tablets a day, as needed.

PRESCRIBE NEOHYDRIN in bottles of 50 tablets. There are 18.3 mg. of 3-chloromercuri-2-methoxy-propylurea in each tablet.

Leadership in diuretic research
Lakeside LABORATORIES, INC., MILWAUKEE 1, WISCONSIN

for relief of

ARTHRITIS

and allied disorders

BUTAZOLIDIN

(brand of phenylbutazone)

NEW SYNTHETIC NON-HORMONAL

A totally new concept in management of rheumatic disorders, treatment with BUTAZOLIDIN offers a combination of clinical advantages not shared by any other agent.

Relieves pain in approximately 3 of every 4 cases within a few days of commencing treatment

Produces functional improvement in many cases by reducing swelling and spasm and increasing mobility

Has favorable effect in virtually all forms of arthritis and many types of painful musculoskeletal disorders

Maintains effectiveness for as long as treatment is continued

Effective by mouth, thus well adapted to routine use in either bedridden or ambulatory patients

In order to secure optimal results with minimal risk of side reactions physicians are urged to send for the brochure "Essential Clinical Data on BUTAZOLIDIN" and other informative literature.

BUTAZOLIDIN® (brand of phenylbutazone) is available as coated tablets of 200 mg. and 100 mg.

A selection from the bibliography on BUTAZOLIDIN . . . (1) Fresberg, R.; Kidd, E. C., and Boyce, K. C.: Studies of Butazolidin and Butapyrin in Patients with Rheumatic Diseases. Paper read before the Annual Meeting of the American Rheumatism Association, Chicago, June 6, 1952. (2) Kuzell, W. C., and others: Phenylbutazone (Butazolidin) in Rheumatoid Arthritis and Gout. J.A.M.A. *149*:729, 1952. (3) Kuzell, W. C., and Schaffarzick, R. W.: Butapyrin in Gout. Stanford M. Bull. 9:194, 1951. (4) Kuzell, W. C., and Schaffarzick, R. W.: Phenylbutazone (Butazolidin), Bull. Rheumat. Dis. *1*:23, 1952. (5) Kuzell, W. C., and Schaffarzick, R. W.: Phenylbutazone (Butazolidin) and Butapyrin in Arthritis and Gout. California Med. *77*:319, 1952. (6) Smith, C. H., and Kunz, H. G.: Butazolidin in Rheumatoid Disorders. J. M. Soc. New Jersey *49*:306, 1952. (7) Steinbrocker, O., and others: Phenylbutazone Therapy of Arthritis and Other Painful Musculoskeletal Disorders. J.A.M.A. *150*:1087, 1952. (8) Stephens, C. A. L., Jr., and others: Benefits and Toxicity of Phenylbutazone (Butazolidin)® in Rheumatoid Arthritis. J.A.M.A. *150*:1084, 1952.

GEIGY PHARMACEUTICALS
Division of Geigy Company, Inc., 220 Church St., New York 13, N. Y.
In Canada: Geigy (Canada) Limited, Montreal

International

RECORD OF MEDICINE

VOL. 166 NO. 6 • WHOLE NUMBER 2844 • JUNE 1953

The Experimental and Clinical Evaluation of l-Arterenol, A Hormone of the Adrenal Medulla*

Maurice L. Tainter, M.D., D.Sc.†

RENSSELAER, N. Y.

Although various discoveries during the nineteenth century, particularly those of Langley, prepared the way for understanding the physiologic importance of the autonomic nervous system, real progress may be said to begin with the present century. The importance of the adrenal gland was emphasized by observations of Oliver and Schäfer[1] and Szymonowicz[2] who obtained extracts from the medullary portion which, when injected intravenously, caused a marked rise in arterial blood pressure, this resulting from a peripheral action of the injected material. Lewandowsky[3] showed that these extracts mimicked the action of the sympathetic nervous system, an observation which was confirmed by Langley[4] and by Elliott.[5] Epinephrine was isolated in pure form from medullary extracts by Abel and Crawford,[6] von Fürth,[7] Takamine,[8] and Aldrich[9] and synthesized by Stolz[10] and by Dakin.[11] Resolution was effected by Flächer.[12]

The therapeutic possibilities of epinephrine were recognized early. Adrenal extracts were in use to control hemorrhage, relieve asthma and to prolong local anesthesia by 1904.[13–15] The development and introduction of synthetic epinephrine substitutes progressed rapidly after the classical investigations of Barger and Dale,[19] and to date more than 200 sympathomimetic amines have been prepared and their pharmacologic properties described.[20] Those of greatest therapeutic importance were reviewed in 1941,[21] so that information up to that time does not need to be discussed here. I would like, within the limits of the space available, to review some of the more recent developments.

* Presented before the Cuban Academy of Science, Havana, Cuba, December 13, 1951.

† Director, Sterling-Winthrop Research Institute, Rensselaer, New York.

Arterenol (nor-epinephrine) is one of the oldest and at the same time the newest of our sympathetic drugs. Synthesis of the racemic compound was described by Stolz[10] and Flächer,[12] but resolution into its optical isomers was only recently successful after years of continued effort in our Institute.[22] Numerous investigations had indicated the presence in biologic preparations of some sympathetic ergone which differed in certain important respects from epinephrine and which resembled the postulated activities of l-arterenol (reviewed, von Euler[23]). Goldenberg *et al*[24]

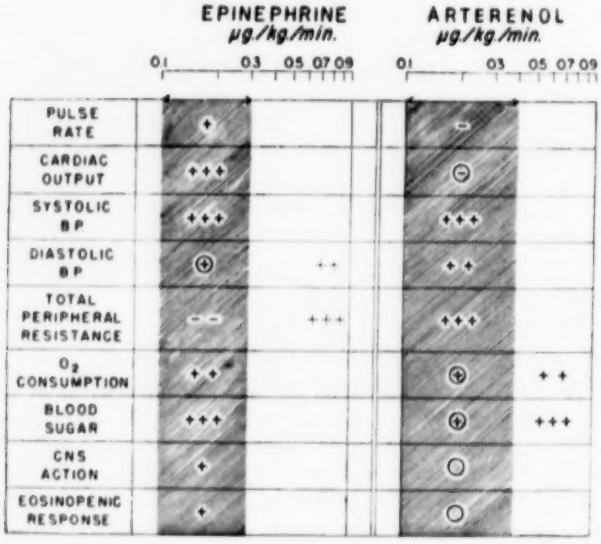


FIG. 1. Comparison of effects of continuous intravenous infusion of epinephrine and Levophed.

(Taken from M. Goldenberg, H. Aranow, Jr., A. A. Smith, and M. Faber, Arch. Int. Med., 86:823, 1950)

and von Euler *et al*[25, 26] presented evidence indicating the presence of this hormone in the adrenal medulla. Subsequently, chemists in our Institute isolated it from commercial epinephrine in pure form, where it constitutes 10-18 per cent of the total.[27, 28] This companion hormone of the adrenal medulla is now produced synthetically and has been made available to the clinician under the trade-marked name levophed®.

The clinical evaluation of levophed® has disclosed several important pharmacologic differences from epinephrine which appear to be of considerable therapeutic importance. The cardiovascular actions of these two drugs have been summarized by Goldenberg *et al*[29] as shown in Figure 1. By contrast with epinephrine, levophed® does not increase cardiac output or pulse rate but does increase total peripheral resistance. Sutton *et al*[30] determined the effect of slow intravenous injection of levophed® into 26 normal adult individuals with the results shown in Table I. It

should be noticed that with the elevation of systolic and diastolic pressures, there was a marked reduction in heart rate. Thus, at the highest dose level of 0.02 mg./min., the blood pressure increased, on the average, 41.5 27 mm. Hg simultaneously with a reduction in pulse rate of 23 beats/min. This has been confirmed by Bayer *et al*.[31] Epinephrine, in doses easily tolerated, usually increased systolic pressure with no change or a reduction in diastolic pressure and caused an increase in pulse rate.[32–34] These differences are more easily understood if one examines the differences in action on the various vascular beds. Blood flow through skeletal muscle and splanchnic vessels is increased by epinephrine and decreased or unchanged by levophed®.[34–36] Both drugs constrict cutaneous blood vessels but that induced by epinephrine is more intense.[36, 37] These findings suggest that arterenol produces some constriction throughout the whole vascular area, whereas that induced by epinephrine is a "patterned" response with constriction in some areas and dilatation in others, the net resultant being a reduction in peripheral resistance in most instances.[32] The reduction in pulse rate, observed with arterenol, is a reflex effect resulting from the increase in peripheral resistance. In passing, it may also be noted that the metabolic effects of arterenol are negligible. The elevation of blood sugar and increased oxygen consumption which characterize the action of epinephrine are not observed.[38]

These differences in action have suggested to von Euler[33] that levophed® is the sympathetic ergone for general physiologic function whereas epinephrine acts as an adjuvant for more special purposes. As previously suggested by Cannon,[39] epinephrine may be an emergency hormone which aids in bringing about rapid adjustment to stressful situations. If this assumption of von Euler is correct, we should expect that levophed® would be useful in maintaining vascular tonus in those conditions where there has been some interruption of tonic sympathetic activity. Recent clinical experience has provided ample evidence of the correctness of this assumption. Wilson and Bassett[40] have described the use of levophed® in 112 patients undergoing

TABLE 1

Effect of Dosage of l-Nor-l-epinephrine upon Blood Pressure and Heart Rate

	0.007 mg./min. (10 cases)	0.01 mg./min. (10 cases)	0.014 mg./min. (9 cases)	0.02 mg./min. (6 cases)
Mean of maximum systolic elevation	16.2 mm./Hg	13.2	21.1	41.5
Mean of maximum diastolic elevation	13.5 mm./Hg	18.3	20.0	27.0
Range of maximum systolic elevation	5.22 mm./Hg	0.45	5.50	25.72
Mean of maximum decrease in heart rate (beats per min.)	−9.3	−17.9	−17.0	−23.0

Taken from Sutton, G. C., A. Kappert, A. Reale, C. H. Skoglund and G. Nylin: Studies on l-nor-epinephrine: Relation of dosage to pressor and bradycardia effect. J. Lab. Clin. Med., 36:460, 1950.

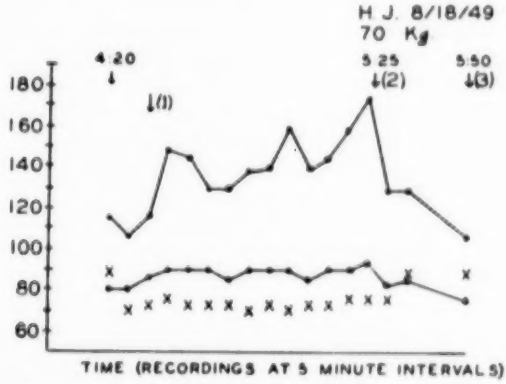
splanchnicectomy and lower dorsal sympathectomy under avertin* anesthesia supplemented with nitrous oxide and/or ether. Operations were begun 5 to 10 minutes after starting the infusion of levophed* in 5 per cent glucose, the rate of infusion being determined by the blood pressure level. A satisfactory blood pressure was maintained during operation without transfusions or supplementary vasopressor agents. Deterling and Apgar[41] have obtained similar results during 36 stages of thoracolumbar sympathectomy performed in an unselected group of 21 patients. The anesthetic agent was ether-oxygen in 30 of the operations with pentothal* nitrous oxide-oxygen in six. With continuous infusion of 0.1-0.3 μg./Kg./min. of levophed*, it was possible to maintain satisfactory blood pressures. The results obtained in a representative case are shown in Figure 2. It should be noted that interruption of the infusion resulted in a prompt fall of blood pressure to shock levels.

Adrenal medullary tumors or pheochromocytomas are characterized by active secretion of the medullary hormones with resultant symptoms of hyperactivity of the sympathetic nervous system, among which persistent hypertension is a common finding. Surgical removal frequently causes a sudden and profound hypotension.[42, 43] Pantridge and Burrows[44] have described the successful removal of a pheochromocytoma in a 66 year old woman. During the 19 minutes after clamping the tumor pedicle, 40 cc. of a solution containing 10 μg. of levophed*/cc. was given intravenously with a resultant restoration of blood pressure to safe levels. One-half hour postoperatively, a levophed* drip was started and the rate of flow adjusted to maintain blood pressure at not less than 90 mm. Hg. After 30 hours it was possible to discontinue infusion without serious hypotension. It is not improbable that the infusion acted as a temporary replacement of the tumor secretion which had been suddenly removed, thus allowing a more gradual restoration of the normal mechanisms of peripheral vasomotor tone.

Bittrich and Mayer[45] and others have shown that intravenous infusions of levophed* are equally effective in maintaining blood pressure after the administration of a spinal anesthetic. This may be illustrated by the following case taken from the Institute files. During the course of a high spinal anesthesia, the patient went into shock and his blood pressure fell from 140/80 to 50/?. At this point, levophed* infusion was begun and within five minutes the blood pressure had increased to 140/70. The anesthetic, which is considered to be responsible for this case of shock, reached the sixth cervical vertebra. Postoperatively, the patient again went into shock and lost consciousness, but consciousness was restored and blood pressure elevated with the use of intravenous infusions of levophed* and 100 per cent oxygen by bag and mask in about five minutes.

The importance of epinephrine in combination with a local anesthetic for prolonging anesthetic action was recognized very early.[15, 16] Subsequent research has led to many vasoconstrictor-local anesthetic combinations. Recent investigations by Dobbs[46] and by Kretchmer and Adriani[47] have shown levophed* to be among the most potent of these potentiators. The latter investigators determined the relative potencies of vasoconstrictors on the duration of spinal anesthesia with procaine by the "saddle block" technic and rated them, in the order of decreasing

potency, epinephrine, posterior pituitary extract, levophed® and ephedrine. No postoperative sequelae were observed nor were any undesirable pressor effects observed. Ausherman[48] has obtained spinal anesthesia with pontocaine® plus levophed® combinations lasting as long as six–ten hours, whereas the control group receiving pontocaine® without a vasoconstrictor had adequate anesthesia for only two–four hours. He reports further that levophed® has been successfully used to



BLOOD SUGAR (1) 105 mg (2) 124 mg (3) 128 mg

AT (1) THE RATE OF INFUSION WAS INCREASED FROM 60 DROPS TO 180 DROPS PER MINUTE. (15 DROPS PER cc) SALINE SOLUTION CONTAINING 2 cc. (2 mg) OF ARTERENOL PER 1000 cc

AT (2) THE I.V. WAS DISCONTINUED

X — PULSE RATE

FIG. 2. Effect of Levophed on blood pressure and blood sugar in patient at (1) 12 cc. per minute of 1:500,000 intravenously; at (2) infusion stopped.

(Taken from C. M. Wilson and R. C. Barrett, University of Michigan Med. Bull., 16:57, 1950)

prolong brachial plexus block, the increase in duration being 100–200 per cent. These data suggest that levophed® will take its place along with epinephrine, cobefrin® and neo-synephrine® as a useful adjuvant to local and spinal anesthetics.

We have previously referred to peripheral vascular collapse resulting from interruption of tonic sympathetic nerve impulses. However, in secondary or hematogenic shock there is an elevated sympathetic activity wherein epinephrine-like agents are not generally considered to be of therapeutic value.[49–55] Recent results obtained with levophed® suggest that some revision of our ideas is required. Let me illustrate this by a recent case history. A male, 20 years of age, underwent a laparotomy because of ileocecal ulceration with fistula formation. An ileo-transverse colostomy with resection of the ileum was done. He went into shock postoperatively, with skin cold and clammy, the pulse 120, and the blood pressure 82/60. He had received 1000 cc. of blood and 1300 cc. of glucose and water during the operation.

An additional 500 cc. of blood failed to bring the patient out of shock. At this juncture, levophed® was administered (8 mg. in 1000 cc.) with a prompt rise of the blood pressure. When levophed® was discontinued for a period of 10 minutes and 500 cc. of blood started, the pressure again fell to shock levels. Infusion of levophed® was able to maintain the blood pressure at proper levels with the disappearance of all signs of shock. After about eight hours, when the levophed® infusion had been discontinued, the pressure again dropped to shock levels (74/38 mm. Hg) in spite of the administration of 500 cc. of blood. The infusion of levophed® promptly re-established a normal peripheral vascular state.

Similar results have been reported in patients varying in age from 20-73 years and representing a cross section of surgical practice. It is apparent that in these patients there are some important differences from those reported for classic shock. One of the most obvious of these is that circulating blood volume had been wholly or in part restored by the administration of fluids, plasma or whole blood. There is another difference, referred to in the early part of this presentation, which is probably important here. Epinephrine, which is secreted in stressful situations,[50] produces a "patterned" vasoconstriction in which the intramuscular vascular bed is unchanged or increased. On the other hand, intense vasoconstriction has been observed in the extremities[56] and in the splanchnic-portal circulation.[57] It is generally believed that prolonged constriction in this latter area leads to "irreversible" shock. This view is supported by the experimental findings of Frank *et al*,[58] Remington *et al*[62] and others who have shown that alteration of this pattern by the administration of sympatholytic agents greatly reduces mortality. Similar results may be obtained if adequate circulation is maintained through the portal circulation.[59] Levophed® induces a general vasoconstriction including the intramuscular blood vessels. The shrinking down of this large vascular area and the circulation through the constricted areas at increased pressure may well increase splanchnic-portal circulation and thereby delay or prevent irreversible shock.

That these recent concepts in the treatment of surgical shock may save many lives is brilliantly exemplified by the recent case report of Luger, Kleiman and Fremont.[60] These physicians treated a 73 year old patient whose gastric ulcer had perforated 24 hours before admission to the hospital. When first seen he was in profound shock with blood pressure so low as to be immeasurable. After three hours of treatment with oxygen and 2250 cc. of blood, plasma, and dextrose intravenously, his circulation was not noticeably improved. Then infusion of levophed® was begun. The blood pressure was promptly restored to normal levels within two minutes, and was maintained by the levophed® for four hours, when he was in good enough condition for laparotomy. During the operation and for 32 hours subsequently levophed® was used almost continuously, since his pressure promptly fell to shock levels whenever the infusion was interrupted. Finally, after that time, it became possible to stop the infusion as his circulatory bed gradually became able to maintain a more normal vascular tonus.

Luger, Kleiman and Fremont state that levophed® provides vasomotor tone in the shock patient and does not prevent the repair of the normal vasomotor mechanisms following shock; that its action is prompt, predictable and easily controlled,

and in their patient, life saving. They conclude that "it seems a powerful addition to therapy."

This conclusion suggests that, in this field as in many others, medical science is now reaping the fruits of many decades of research carried out in many parts of the world. It has been a long search. We may look back to the moment 95 years ago when Vulpian for the first time saw the "chromaffin substance" in the suprarenal gland. He may well have pondered on the chemical nature and the physiologic role of this new substance, but many years of painstaking work had to pass before one of the "chromaffin substances" was isolated; then it appeared that with the discovery of epinephrine the search was over, the goal had been reached. They did not know then what was discovered only recently; that is, the existence of a second chromaffin substance, l-arterenol, so elusive that, undetected, it followed natural epinephrine like a shadow through all processes of purification.

We may ask ourselves whether this search has actually reached its goal, and we may try to look into the future to the tasks that lie ahead. Neither the mechanisms which regulate the production of l-arterenol, nor all its therapeutic possibilities are completely known at the present time, and the intimate mechanisms by which this hormone and epinephrine produce enormous energy changes in the microcosmos of the body cells is still as obscure as it was 50 years ago.

The discoveries of the past have given to the present generation an impressive scientific background and the tools to carry on, but at the same time they have revealed the boundaries of large areas of *terra incognita*. Its exploration is the task ahead, to success in which we may look forward with confidence. We know that nature does not willingly yield its secrets, but we also know that she has to contend with man's unquenchable thirst for knowledge. Our abiding faith in man's ability to unravel nature's secrets has never been expressed better than in the words of that great poet, Amado Nervo.

Revelación

Deja que los seres y las cosas hablen;
si sabes mirarlos y escucharlos bien,
te dirán los cínifes por qué te desangran,
te dirá la abeja por qué acendra miel,
te dirá la rosa por qué te perfuma,
te dirán las olas por qué su vaivén,
te dirá el cometa cuál de sus remotas
peregrinaciones el misterio es.

. . . Y la propia Esfinge, si arrostras impávido,
si contemplas firme su glacial mudez,
venderá su enigma . . .
Ni los dioses vencen
la perseverancia de un tenaz ¡por qué!

BIBLIOGRAPHY

1. Oliver, G., and Schäfer, E. A.: On the physiological action of extract of the suprarenal capsules; the physiological effects of extracts of the suprarenal capsules, J. Physiol. *17*:ix, xiv, 1895; *18*:230, 1895.
2. Szymonowicz, L.: Arch. f. d. ges. Physiol. *64*:97, 1896 (Trendelenburg, P.: Adrenalin und adrenalinverwandte Substanzen, Handb. Exper. Pharmakol., A. Heffter *2.2*:1177, 1924).

3. Lewandowsky, M.: Wirkung des Nebennieren extractes auf die glatten Muskeln der Haut, Zentralbl. f. Physiol. *14*:433, 1900.
4. Langley, J. N.: Observations on the physiological action of the suprarenal bodies, J. Physiol. *27*:237, 1901–02.
5. Elliott, T. R.: The action of adrenalin, J. Physiol. *32*:401, 1905.
6. Abel, J. J., and Crawford, A. C.: On the blood-pressure raising constituent of the suprarenal capsule, Bull. Johns Hopkins Hosp. *8*:151, 1897.
7. von Fürth, O.: Zur Kenntniss der brenzcatechinähnlichen Substanz der Nebennieren, Ztschr. f. physiol. Chem. *29*:105, 1899.
8. Takamine, J.: The blood-pressure-raising principle of the suprarenal glands: a preliminary report, Therap. Gaz. *27*:221, 1901.
9. Aldrich, T. B.: Adrenalin, the active principle of the suprarenal gland, J. Am. Chem. Soc. *27*:1074, 1905.
10. Stolz, F.: Ueber Adrenalin und Alkylaminoacetobrenzcatechin, Ber. d. deutsch. chem. Gesellsch. *37*:4149, 1904.
11. Dakin, H. D.: On the physiological activity of substances indirectly related to adrenalin, Proc. Roy. Soc. London, S. B. *76B*:491, 498, 1905.
12. Flächer, F.: Ueber die Spaltung des synthetischen dl-Suprarenins in seine optisch aktiven Komponenten, Ztschr. f. physiol. Chem. *58*:189, 1908.
13. von Frisch, A.: Adrenalin in urological practice, Medical Age (Detroit, Michigan), Sept. 10, 1902 (J. A. M. A. *39*:864, 1902).
14. Floersheim, S.: The use of the suprarenal extract in diseases of the heart and lungs, N. Y. State J. Med., July, 1902 (J. A. M. A. *39*:282, 1902).
15. Menger, R.: Adrenalin chloride and hydrochlorate of cocain in dentistry, Texas Med. J., Oct. 1903 (J. A. M. A. *41*:1233, 1903).
16. Braun, H.: Zur Anwendung des Adrenalins bei anesthesierenden Gewebs-Injektionen, Centralbl. f. Chir., 1903 (J. A. M. A. *41*:993, 1903).
17. Reilly, T. F.: Suprarenal extract by spray and cotton tampon to the nasal chambers with good results in asthma, J. A. M. A. *42*:1475, 1904.
18. Voigt, B.: Adrenalin am Krankenbett, Munchen. med. Wchnschr., 1904 (J. A. M. A. *42*:1327, 1904).
19. Barger, G., and Dale, H. H.: Chemical structure and sympathomimetic action of amines, J. Physiol. *41*:19, 1910–11.
20. Lands, A. M.: Review of the structural requirements for sympathomimetic drug action. First Symposium on Chemical-Biological Correlation, May 26–27, 1950, National Academy of Sciences—National Research Council, Washington, D. C., 1951, pp. 73–123.
21. Tainter, M. L.: Sympathomimetic amines as epinephrine substitutes, J. A. M. A. *116*:2769, 1941.
22. Tullar, B. F.: The resolution of dl-arterenol, J. Am. Chem. Soc. *70*:2067, 1948.
23. von Euler, U. S.: Hormones of the sympathetic nervous system and the adrenal medulla, Brit. M. J. Jan. 20, 1951.
24. Goldenberg, M.; Faber, M.; Alston, E. J., and Chargaff, E. C.: Evidence for the occurrence of nor-epinephrine in the adrenal medulla, Science. *109*:534, 1949.
25. vonEuler, U., Hamberg, U.: l-nor-Adrenaline in the suprarenal medulla, Nature, London. *163*:642,1949.
26. Bergstrom, S.; von Euler, U. S., and Hamberg, U.: Isolation of nor-adrenaline from the adrenal gland, Acta chem. Scandinav. 3:305, 1949.
27. Tullar, B. F.: The separation of l-arterenol from natural U.S.P. epinephrine, Science. *109*:536, 1949.
28. Auerbach, M. E., Angell, E.: The determination of arterenol in epinephrine, Science. *109*:537, 1949.
29. Goldenberg, M.; Aranow, H., Jr.; Smith, A. A., and Faber, M.: Pheochromocytoma and essential hypertensive disease, Arch. Int. Med. *86*:823, 1950.
30. Sutton, G. C.; Kappert, A.; Reale, A.; Skoglund, C. H., and Nylin, G.: Studies on l-nor-epinephrine: relation of dosage to pressor and bradycardia effect, J. Lab. & Clin. Med. *36*:460, 1950.
31. Bayer, O.; Blumberger, K. J., and Effert, S.: Ueber Kreislauf- und Herzwirkungen des Noradrenalins (Arterenol) biem Menschen, Cardiologia. *16*:145, 1950.
32. Goldenberg, M.; Pines, K. L.; Baldwin, E. deF.; Greene, D. G., and Roh, C. E.: The hemodynamic response of man to nor-epinephrine and epinephrine and its relation to the problem of hypertension, Am. J. Med. 5:792, 1948.

33. Barcroft, H., and Konzett, H.: Action of nor-adrenalin and adrenaline on human heart-rate, Lancet. *1*:147, 1949.
34. Swan, H. J. C.: Effect of noradrenaline on the human circulation, Lancet. *2*:508, 1949.
35. de Laroy, C.; Greenfield, A.; McCorry, R., and Whelan, R.: The effects of intravenous infusion of mixtures of l-adrenaline and l-nor-adrenaline on the human subject, Clin. Sc. *9*:71, 1950.
36. Luduena, F. P.; Ananenko, E.; Sigmund, O. H., and Miller, L. C.: Comparative pharmacology of the optical isomers of arterenol, J. Pharmacol. & Exper. Therap. *95*:155, 1949.
37. Kappert, A.; Sutton, G. C.; Reale, A.; Skoglund, K. H., and Nylin, G.: The clinical response of human beings to l-nor-adrenaline and its clinical applicability, Acta cardiol. *5*:121, 1950.
38. McChesney, E. W.; McAuliff, J. P., and Blumbero, H.: The hyperglycemic action of some analogs of epinephrine, Proc. Soc. Exper. Biol. & Med. *71*:220, 1949.
39. Cannon, W. B.: Bodily changes in pain, hunger, fear and rage, Appleton-Century, New York, 1929.
40. Wilson, C. M., and Bassett, R. C.: Maintenance of vasopressor tone with nor-epinephrine in extensive sympathectomy, Univ. Michigan M. Bull. *16*:57, 1950.
41. Deterling, R. A., and Afoar, V.: The use of nor-epinephrine (l-arterenol) as a pressor drug with special reference to thoracic lumbar sympathectomy, Ann. Surg. *133*:37, 1951.
42. Wright, J. L., and Jones, W. C.: Pheochromocytoma simulating essential hypertension; report of a case with successful surgical treatment, South. M. J. *44*:14, 1951.
43. Yarborough, J. A.: Pheochromocytoma; diagnosis and treatment, Am. Pract. *2*:434, 1951.
44. Pantridge, J. F., and Burrows, M. M.: A case of adrenal pheochromocytoma, Brit. M. J. *1*:448, 1951.
45. Bittrich, N. M., and Mayer, G. T.: Spinal anesthesia for urological procedures in the aged, Urol. & Cutan. Rev. *53*:513, 1949.
46. Dobbs, E., DeVier, C.: l-Arterenol as a vasoconstrictor in local anesthesia, J. Am. Dent. A. *40*:433, 1950.
47. Kretchmer, H. E., and Adriani, J.: A comparative study of certain vasoconstrictors on the duration of spinal anesthesia with procaine, South. M. J. *43*:771, 1950.
48. Ausherman, H. M.: Prolongation of spinal anesthesia (75 to 100 per cent) with Levophed intrathecally; a preliminary report, Am. J. Surg. *81*:521, 1951.
49. Freeman, N. E.; Freedman, H., and Miller, C. C.: The production of shock by the prolonged continuous injection of adrenaline in unanesthetized dogs, Am. J. Physiol. *131*:545, 1940–41.
50. Driessens, J.: Etude biologique du choc chirurgical. L'hypertension arterielle paroxyatique secondaire a tout traumatisme tissulaire est duc a une decharge adrenalinique des surrinales, Rev. de chir., Paris. *67*:129, 1948.
51. Wiggers, H. C., Ingraham, R. C.; Roemhild, F., and Goldberg, H.: Vasoconstriction and the development of irreversible hemorrhagic shock, Am. J. Physiol. *153*:511, 1948.
52. Remington, J. W.; Wheeler, N. C.; Boyd, G. H., Jr., and Caddell, H. M.: Protective action of Dibenamine after hemorrhage and after muscle trauma, Proc. Soc. Exper. Biol. & Med. *69*:150, 1948.
53. Remington, J. W.; Hamilton, W. F.; Caddell, H. M.; Boyd, G. H., Jr., and Hamilton, W. F., Sr.: Some circulatory responses to hemorrhage in the dog, Am. J. Physiol. *161*:106, 1950.
54. Remington, J. W.; Hamilton, W. F.; Boyd, G. H., Jr.; Hamilton, W. F., Jr., and Caddell, H. M.: Role of vasoconstriction in the response of the dog to hemorrhage, Am. J. Physiol. *161*:116, 1950.
55. Remington, J. W.; Hamilton, W. F.; Caddell, H. M.; Boyd, G. H., Jr.; Wheeler, N. C., and Pickering, R. W.: Vasoconstriction as a precipitating factor in traumatic shock in the dog, Am. J. Physiol. *161*:125, 1950.
56. Freeman, N. E.; Shaw, J. L., and Snyder, J. C.: Peripheral blood flow in surgical shock; reduction in circulation through hand resulting from pain, fear, cold, and asphyxia, with quantitative measurements of volume flow of blood in clinical cases of surgical shock, J. Clin. Investigation. *15*:651, 1936.
57. Page, I. H., and Abell, R. G.: Effect of acute hemorrhage and of subsequent infusion upon the blood vessels and blood flow as seen in the mesenteries of anesthetized dogs, Am. J. Physiol. *143*:182, 1945.
58. Frank, H. A.; Selioman, A. M., and Fine, J.: Traumatic shock. XIII. The prevention of irreversibility in hemorrhagic shock by viviperfusion of the liver, J. Clin. Investigation. *25*:22, 1946.
59. Cohn, R., and Parsons, H.: Relationship of portal hypertension and irreversibility of shock, Am. J. Physiol. *160*:437, 1950.
60. Luger, N. M.; Kleiman, A., and Fremont, R. E.: Treatment of shock with arterenol, J. A. M. A. *146*:1592, 1951.

Endocrines and Psychiatry*

Francis J. Braceland, M.D., Sc.D.†
HARTFORD, CONN.

In the various fields of medical practice advances have depended not only upon the progress of general knowledge but also upon the development of necessary and adequate technologic advances. Endoscopy is a case in point: it could not have developed until technology had advanced far enough to perfect the requisite apparatus. Surgery moved forward quickly after bacteriology had contributed its leaven. Bacteriology in turn had had to await the development of microscopy, and thus medicine moves forward *pari passu* with advances in other scientific disciplines. In this paper we, as psychiatrists, are interested in the recent advances in endocrinology (due largely to new findings in the field of steroid chemistry). Here again is held forth the intimation that man's behavior might be explained or even modified by the use of new hormonal substances.

Actually the search for hormonal products capable of modifying pathologic behavior is not a new one in psychiatry. It had a broad resurgence following Clarke's paper on the relationship of goiter to insanity in 1887. Soon afterward the use of thyroid substance in psychiatric illnesses went somewhat out of bounds and it was not long before thyroid glands were being removed surgically with the expectation of curing catatonia.

This story was repeated regularly as each new endocrine product appeared—glowing reports, great expectations, claims which could not be substantiated, and then disappointment. In 1946 Stearns, noting this unfortunate cycle, wrote:

"Contemporary with focal infection came endocrine imbalance. The ductless gland lent itself readily to mysticism and speculation and, beautifully aided by the manufacturing pharmacist, the ox and the sheep were exploited in what now seems to have been a forlorn hope."

By now it is obvious to us that the matrix of man's behavior in the widest sense is comprised of factors which are sociologic, economic, cultural, metabolic and physiologic. It is in this context of the whole man that the role which hormones play in modifying behavior becomes evident. They can only be a small part of the whole in man; in animals it is possible for them to play a larger role.

Beach reviewed in exhaustive detail the experimental data which serve as an interpretive basis of the relations between hormones and behavior in animals. He made several observations which are pertinent in our study of the subject in man, namely:

1) None of the behavioral responses thus far investigated has been found to depend upon one and only one hormone.

---

* Reprinted from MD, March–April, 1953.

† Psychiatrist-in-Chief at the Institute of Living, Hartford, Connecticut.

2) Hormones are only one of several factors which operate to produce a particular pattern of behavior and the final form of overt response may be controlled to a greater degree by the environmental stimulus than by hormonal conditions.

3) Many of the experiments and theories dealing with hormonal influences are of little value because the authors fail to recognize the complexity either of the endocrinologic or psychologic side of the picture.

These postulates are of the greatest importance in the understanding of this subject for frequently the internist is questioned regarding the possibility of some mild glandular dysfunction, real or alleged, being at the basis of aberrant behavior. As stated by Beach, there is no one-to-one ratio in the functioning of endocrine glands.

It is obvious that in the vast and complicated inter-relationship which makes up human behavior many intangible factors are at work—magnitude of change, duration of effect, time and tide in hormonal action. An instance of this is found in hypothyroidism: on the amount of deficit, the time of life, the duration of the deficiency depend the final results of the lack of thyroid in the human economy. Also the treatment of cretinism by replacement therapy, which aids markedly in the treatment of the deficiency, often fails to remedy the profound emotional defects which are so well known. This fact in no way lessens the great importance of thyroid in cretinism but it makes the point that correction of a metabolic disorder of itself does not necessarily insure normal mental function.

The clinical symptoms which result from both hypo- and hyperthyroidism vary and there is no strict correlation between the degrees of these symptoms and the extent of the psychiatric symptoms which accompany them. Sometimes the psychiatric symptoms only appear after medical treatment has begun. Indeed, all possible combinations of psychological symptoms are possible in myxedema and hyperthyroidism, from minor difficulties to openly psychotic states. As above, correction of the metabolic difficulty is no guarantee that the mental symptoms will disappear quickly. Obviously, therefore, there is no constant or invariant relationship between hormones and behavior. The psychologic responses to glandular imbalance in the human being are dependent upon the patient's characteristic personality make-up.

As to the time of the illness, it is apparent that that would be important. Even as thyroid deficiency in the new-born would call forth a set of symptoms noticeably different from those of the myxedema of middle age, so also would castration in the male call forth different symptoms if it occurred in childhood, in adult life, at the time of marriage, or in old age. Here not only are the physiologic and anatomic reactions different but also there is necessarily great difference in the psychological reactions called forth in various age groups.

Another very important aspect of this problem should be spoken of at this time, namely that individuals with these endocrine disorders, in contrast to those of normal function, are much more vulnerable to stress of any kind and it is not unusual that the transition from hypo- or hyperfunction to that of normal function is frequently accompanied by an emotional disturbance of major proportions. A good example of this is the patient with Addison's disease, who seemingly is precipitated into an acute psychotic episode after hormonal treatment is started. Despite

the fact that the underlying pathology is corrected and that the adrenal cortical deficiency is remedied, the patient displays gross psychotic symptoms and is apparently much worse off than he was when he was in a state of acute adrenal cortical insufficiency. The same thing happens in Cushing's disease: when the hypercorticism is corrected by surgical removal of the adrenocortical tumor there is seen in some patients a period of profound psychiatric disturbance which does not seem to be related to any demonstrable physiologic imbalance. Upon close examination of these conditions one has the impression that while the level of physiologic adaptation is being rapidly shifted, the over-all pattern of psychological adjustment is being modified accordingly. The implication is that this is an over-all pattern effect and not the result of aberration in a single hormonal modality.

The psychiatrist has to keep in mind when he is called in consultation in these states that the truly significant fact is that a change has occurred and that the homeostatic buffers have apparent limits which, when approached by major changes, are taxed seriously in their capacity to withstand. Hence, at this point, what would be otherwise easily tolerated stress is sufficient to exceed the limits permitted; the ensuing reorganization of the personality differs radically from the previous pattern. Therefore, violent shifts in the internal environment constitute as much of a psychological stress as do apparently traumatic disruptions in the external environment. The time required for emotional adjustment to these great environmental changes is sometimes considerable; during the interim psychological defense mechanisms typical of the individual are mobilized and they constitute the clinical psychiatric picture. Parenthetically, there is a note of warning here for the avid young psychiatrist with a tendency to rush in quickly with a too active form of psychotherapy. This, too, would be dangerous in a situation where the adaptation is tenuous.

Earlier Rome and Braceland studied the psychological effects of ACTH, cortisone and related substances as a part of a more extensive physiological investigation. In view of the widespread usage of these substances and the fact that they are now in the hands of most clinicians, it is important to restate the findings of these investigators here. They group the psychological responses to ACTH and cortisone into four categories and, as yet, have seen no reason for changing their first impressions. Grade one was composed of deviation in mood, usually in the direction of elevation. There were commensurate changes in the pattern of thinking and behavior. Grade two responses were more readily detected merely because they were more pronounced and it was for this reason that euphoria was widely reported to be the typical psychological reaction to the administration of these drugs. Grade three responses were the psychoneurotic reactions to the stress of medication and the clinical forms of personality reaction which were evidenced were indistinguishable from the usual psychoneurotic symptoms evidenced in a wide variety of patients. Grade four designated the psychotic reaction types which were encountered occasionally. Their clinical manifestations varied in accordance with the organization of the patients' previous personalities.

It is incumbent upon the psychiatrist, therefore, and upon the clinician in the examination of any untoward emotional symptoms to determine whether or not patients have been treated with these drugs. Obviously, the psychological manifes-

tations noted could only be as a result of the effect of the hormonal substance upon that particular personality at that particular time and under those particular circumstances. Another reason for the appearance of these symptoms may have been the large doses used at first in the treatment of patients with a variety of conditions.

It is in the emotional disorders of men and women in middle life that the temptation frequently arises to undertake treatment of the patient with a variety of endocrine products. Frequently the implication here is that there must be some glandular imbalance accounting for these psychological symptoms. The belief is growing, however, that endocrinological changes which take place in middle life have little if anything to do with the emotional and mental symptoms evidenced at this time. In the opinion of some investigators there is no justification for the term "menopausal syndrome" if it includes the presence of a psychiatric disorder in its definition. Undoubtedly, a metabolic instability is set up as a result of failing ovarian function and this has its effect upon the autonomic nervous system resulting in that common symptom, the hot flash. The majority of women experience no symptoms of psychiatric nature during the menopause and they handle without difficulty any mild symptoms of autonomic overreactivity. Unquestionably previous psychoneuroses are reactivated and exacerbated at the time of the climacteric but it is quite evident that endocrine and estrogen therapy will be of no benefit in relieving these psychiatric disorders. As to the male in the fifties, here is really a problem. Many men in this age group are prone to depression and to various emotional syndromes. Again, this is frequently blamed upon endocrine deficit and the patient is given large doses of testosterone and other endocrine products. Here again it is most likely that the emotional symptoms are in no way related to endocrine failure but rather are connected with the numerous strains and anxieties which beset the male who is beginning the downward grade.

Not infrequently the clinician is called upon to treat the syndrome of obesity and "nervousness" with thyroid extract, because the patient alleges that treatment with thyroid at an earlier time corrected these symptoms. There are numerous and nebulous statements about former low metabolic rate and a rapid recovery following thyroid extract and the clinician is urged to treat the syndrome with this substance. Many of these patients have elaborated their own theories regarding their illness and rarely, if ever, allow for the possibility that they may be emotionally distressed. Their sophistication grows and they are able to give classical histories of cold sensitivities, skin change, sluggishness, changes in menstrual habits, etc. When to this is added an equivocal elaboratory report in the form of a borderline low metabolic rate, it is tempting to the hurried clinician to tie all these things together and to treat them with thyroid extract. Unfortunately, the clinician accepts the neurotic symptoms as consonant with this type of defect and often the results which are obtained *post hoc* are attributed to the remedy of a nonexistent hormonal deficiency. Many of the beneficial results seen in the treatment of these patients are actually the consequence of suggestion and of the physician-patient relationship.

These statements in no way attempt to negate the usefulness of proper hormonal medication when required, for that would be foolish and unscientific. They do, however, call attention to the fact that many of the conditions assertedly corrected

by the administration of hormonal substance are in actuality responding to the psychotherapeutic concomitants of the treatment.

Several conditions with an interesting congeries of symptoms have definite psychosomatic connotations and are frequently seen earliest by the psychiatrist. The first is hypoglycemia, because a majority of the symptoms which occur in this state are nervous and mental in nature. No single psychiatric syndrome dominates this mental picture; the symptoms range over the entire psychiatric spectrum and one can see anything from deep coma to violence. Attacks of hypoglycemia have been confused with drunkenness, neuroses, psychoses, epilepsy and brain tumor. The symptoms, usually most marked after a nocturnal fast, frequently have the habiliments of a toxic confusional state and disappear rapidly after an injection of dextrose.

Portis, a gastroenterologist, has stated that most psychoneurotic patients who suffer from chronic fatigue have hypoglycemia as an integral factor in it. He believes that this hypoglycemia and a consequent fatigue result from some emotional states, caused by a loss of spontaneous zest and a revulsion against routine activities. Apparently the emotional tensions known as zest, enthusiasm or interest help keep up the tone of the vegetative innervations. In chronic fatigue of this type, therefore, while the hypoglycemia would be the basic phenomenon, the mental and emotional reactions again would depend upon the person involved.

Occasionally the psychiatrist is the first to see another type of patient, eventually found to have a tumor of the head or body of the pancreas. Mental and emotional symptoms accompany some of these growths with sufficient regularity to alert us to their significance. Whether these symptoms have hormonal relationships is unknown but the syndrome they make up is important, for it frequently antedates the appearance of the physical symptoms by several months. Yaskin first called attention to this phenomenon. He noted that a psychiatrist frequently saw these patients in the early stages and that the anxiety and that the ***depressive symptoms became ameliorated after the physical symptoms supervened***. The diagnostic importance of this progression in time is obvious. The syndrome is made up as follows: (1) obstinate insomnia not relieved by somnifacients; (2) depression with crying spells and marked anxiety, which everyone but the patient considers to be of nervous origin; (3) striking anxiety, unrelieved by rest and sedation, in which the patient has the feeling of impending disaster; (4) a feeling of depression, without the feeling of unreality, in patients who are pallid and sallow and who have abdominal pain. This combination of symptoms, properly interpreted, opens to the psychiatrist a new field of endeavor and of usefulness to the internist and surgeon.

Obviously then, hormones are important factors in the matrix of human emotions and human behavior. As yet, they cannot be intimately connected with the appearance of specific emotional symptoms, tempting as it is to try to connect them. We are aware of the fact that Freud once said that some day all of the things that he was talking about would be treated by hormones or similar substances; but that day has not yet arrived. One may hope that future research will shed much more light upon this subject.

Pan American Medical Woman's Journal

ASSOCIATE EDITOR
CATHERINE H. ROTH, M.D.
New York City

EDITOR-IN-CHIEF
ELIZABETH MASON-HOHL, M.D.
1234 No. Vermont Ave.
Hollywood 27, California

ASSOCIATE EDITOR
ALMA DEA MORANI, M.D., D.N.B., F.A.C.S., F.I.C.S.
Philadelphia, Pennsylvania

Terramycin Therapy In Burns

H. D. Ritchie
A. B. Wallace
UNIVERSITY OF EDINBURGH,
EDINBURGH, SCOTLAND

An attempt has been made to assess the effect of the antibiotic, terramycin, in the treatment of burns and scalds by the exposure method in children[1] and to compare its efficacy with that of penicillin. The drug was given to 50 consecutive burnt or scalded children admitted to the Royal Hospital for Sick Children, Edinburgh.

Terramycin was first extracted from the *Streptomyces rimosus* by Finlay and his colleagues[2] in January, 1950, in New York. It is effective against a wide range of organisms, including most of the gram-positive and gram-negative bacteria, spirochetes, rickettsia, some of the larger viruses, and *Entamoeba histolytica*.

In the treatment of burns and scalds, its activity against the various strains of *Staphylococcus aureus*, *Streptococcus hemolyticus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas pyocyaneus* is perhaps of the most importance. It has little or no action on *Bacillus proteus* and will control *Ps. pyocyaneus* only in strong concentration.

EFFECTIVE CONCENTRATIONS

The concentration of the drug and the number and virulence of the organisms will, of course, affect the action. According to Bliss et al,[3] bactericidal action does not occur under the minimal inhibitory concentration of 4 mg. per milliliter. In concentrations of 4 micrograms per milliliter, terramycin is considered bacteriostatic and in higher concentrations bactericidal.

ABSORPTION AND EXCRETION

Following oral administration, the drug is well absorbed and absorption-excretion studies in man[4] show that maximal blood levels are attained in two to four hours, while after six hours the levels fall below the bacteriostatic range.

It is not possible to produce a significant increase in the blood level in adults by giving doses in excess of 1 Gm. six-hourly.[5,6] This is believed to be due to the inability of the gut to absorb further quantities of the drug which are passed unchanged

Reprinted from Antibiotics and Chemotherapy, Vol. II, No. 8, August, 1952.

in the feces. However, it seems that, from the blood levels obtained in the children in this series, the same may not be true in the younger age groups. Terramycin is excreted chiefly in the urine although, after oral administration, a large proportion remains unabsorbed, particularly if antacids, such as aluminium hydroxide, are being taken concurrently.[7] Recently, it has been shown that sodium bicarbonate does not interfere with the absorption of the drug and that normal blood levels are obtained when this is being taken.[8]

DISTRIBUTION OF TERRAMYCIN

Terramycin is widely dispersed throughout the body in much the same fashion as are aureomycin and chloramphenicol. According to Welch,[5] the concentration of terramycin in the skin of animals is several times that in the blood and if this were the case in man also it would be of particular importance in the treatment of scalds or cutaneous infections.

ADMINISTRATION AND DOSAGE

The dosage given followed the recommendations of Werner et al:[9] 50 to 100 mg. per Kg. of body weight per day in the adult. In this series of children the dose was:

Below 3 years	250 mg. 6-hourly
From 3 to 6 years	375 mg. 6-hourly
From 6 to 12 years	500 mg. 6-hourly

The drug was given for a period of five days.

Terramycin is stated to be too irritant for intramuscular or subcutaneous injection, but we have used the drug intravenously in a few children of 3 years and upwards when it could be added to an intravenous infusion which was being given for other reasons. So far, there have not been any reactions in this method, and the veins did not appear to be damaged.

TOLERATION

The drug was taken orally by the children without difficulty. In most patients under two years of age, the elixir was given. Children over two years of age were given the contents of 250-mg. gelatin capsules in milk.

TOXIC EFFECTS

The toxic effects reported most commonly are those of alimentary intolerance, that is, nausea, vomiting, and diarrhea. Epigastric pain, presumably due to gastritis, is described and also stomatitis, vertigo,[10] and a maculo-papular rash going on to exfoliation.

In our series, reactions occurred in 11 cases (22 per cent). Nine of these had nausea and vomiting and were treated with sodium bicarbonate, 10 Gm., which was given 20 minutes before the terramycin was administered. This permitted continuation of terramycin therapy in 7 cases, but in 2 cases (4 per cent) vomiting continued

and terramycin had to be stopped. In the other 2 cases, a generalized morbilliform rash appeared on the third day; the rash faded within 48 hours, without the exfoliation described in the literature, and no papular stage was observed. Looseness of the stools was present in most cases but did not cause any upset.

A comparison of the series reported by Finland et al,[11] and Schoenbach et al,[4] with the present series is shown in table I.

In Finland's series, the dosage seems to have been variable and administration sometimes prolonged.

It is worth noting, however, that few of the children in the present series were seriously ill and this, perhaps, to some degree modified their reactions.

TABLE I
Toxic Reactions

Series	Number of Cases	Percentage of Cases with Toxic effects	Percentage of Cases in whom Drug Was Stopped
Finland et al[11]	87 adults	56	13
Schoenbach et al[4]	36 adults	50	?
Present series	50 children	22	4

According to Pulaski,[12] clinical allergic reactions to penicillin occur in between 1 and 2 per cent of cases treated, a figure which is much lower than that quoted for terramycin in adults. Repeated intramuscular injections, however, are not well tolerated by children and, for example, in extensive burns of the buttocks and legs, the available muscles in a child of 2 years are few and soon converted into fibrous masses from which the amount absorbed is doubtful. As more than 50 per cent of burns and scalds are sustained by children below 2 years of age,[13] an effective antibiotic which can be given orally is desirable.

Special Investigation on Terramycin Series

Blood serum assay was carried out on 30 of the children with the following results:

Average level: At six hours after first dose—5.5 micrograms
Before penultimate dose—5.9 micrograms
Minimum level: 1 microgram per milliliter
Maximum level: 20 micrograms per milliliter

The average figures are of the order reported in adults, but the final blood serum assay showed some figures up to 20 micrograms per milliliter, which are higher than any reported in adults. This may be due to the comparatively large absorptive surface in children, i.e., the ratio—

intestinal absorptive surface/body weight

In 7 patients (24 per cent), the blood serum assay level fell below the bacteriostatic level of 4 micrograms per milliliter. In 3 the specimens may have deteriorated

while awaiting bacteriologic assay, but, if from the claims of Welch[6] in animal experiments the skin concentration is in fact higher than the blood level, the actual concentration of the antibiotic reaching the affected area may have been within the desired range. Furthermore, the initial samples were withdrawn at six hours by which time blood levels may have begun to fall slightly.[4]

URINE ASSAY

This was done in 18 patients and satisfactory levels were obtained in all instances:

Average level: 450 micrograms per milliliter

Minimum level: 90 micrograms per milliliter

Maximum level: 1000 micrograms per milliliter

The urine concentrations were also higher than those reported in adults.

Bacteriology

The burnt or scalded area was swabbed immediately after cleansing, 48 hours later, and at the end of therapy.

In 71 per cent of the burns or scalds, a positive bacteriologic report was obtained at some time during treatment. *Staphylococcus aureus* was by far the commonest pathogen with, in decreasing order of frequency, hemolytic *Streptococcus*, *Staphylococcus albus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Streptococcus faecalis*. From two burn surfaces *Bacillus proteus* was grown and from one *Ps. pyocyaneus*. This is the typical picture of the bacteriology of burns and scalds treated by the exposure method. Infection with *B. proteus* and *Ps. pyocyaneus* was not seen, and this may probably be attributed to the cool, dry, and well-oxygenated conditions found in an exposed case, rather than to prophylaxis with antibiotics.

COMPARISON OF PENICILLIN AND TERRAMYCIN SERIES

Penicillin

Over 230 cases have now been treated in the Royal Hospital for Sick Children, Edinburgh, by exposure and systemic penicillin; 300,000 international units per day being the usual dose. This has been supplemented by the local insufflation of penicillin-lactose powder (10,000 international units per Gm.). There have been no skin reactions from using the powder; the method has proved to be satisfactory and has stood the test of time. The incidence of infection is low, being about 15 per cent of cases treated,[13] and it has always been mild, low-grade, and of a local variety only.

Terramycin

Fifty consecutive patients with burns and scalds were treated. In these the most extensive injuries involved 22 per cent of the body surface. In a few cases the burns were deep, but the majority were superficial in type. Blisters were snipped and the burnt area and surrounding skin cleaned with Cetrimide, 1 per cent. The burn was then washed with sterile 0.9 per cent saline and dried. No local powder of any kind

was applied, and the burns were exposed to the air of the ward. Crusting occurred within the customary 48 hours, and the healing time was within normal limits for exposure. As stated above, positive bacteriologic reports were obtained in 71 per cent of the cases but in none of these did any local manifestation of infection develop.

TABLE II

Series Treated at Royal Hospital for Sick Children, Edinburgh

Antibiotic	Number of Cases	Percentage of Cases with Mild Local Infection	Percentage of Cases with Toxic Effects	Percentage of Cases in Whom Drug Was Stopped	Healing Time
Penicillin	230	15	nil	nil	26 days
Terramycin	50	nil	22	4	27 days

Table II shows a comparison of our results in these two series.

CONCLUSIONS

As might be expected from the breadth of its bacterial spectrum, terramycin appears to be a more efficient prophylactic agent than penicillin in the treatment of burns and scalds. It is well tolerated by children, and bacteriostatic levels are reached in most cases. It has the advantage that it can be given orally. It would appear to be better tolerated by children than by adults.

ACKNOWLEDGMENTS

Acknowledgment is made to Dr. Ian C. Gould, Bacteriology Department, University of Edinburgh, for his help in the drug assays.

Supplies of terramycin were kindly arranged by Dr. G. L. Hobby, of Chas. Pfizer, & Co., Inc., Brooklyn, New York.

BIBLIOGRAPHY

1. Wallace, A. B.: The exposure treatment of burns, Lancet 1:501, (March) 1951.
2. Finlay, A. C.; Hobby, G. L.; P'an, S. Y.; Regna, P. P.; Routien, J. B.; Seeley, D. B.; Shull, G. M.; Sobin, B. A.; Solomons, I. A.; Vinson, J. W., and Kane, J. H.: Terramycin, new antibiotic, Science 3:85, (Jan. 27) 1950.
3. Bliss, E. A.; Warth, P. T., and Chandler, C. A.: Susceptibility of gram-positive cocci, gram-negative bacilli, and clostridia to terramycin, Ann. New York Acad. Sc. 53:277, (Sept. 15) 1950.
4. Schoenbach, E. B.; Bryer, M. S., and Long, P. H.: Pharmacology of terramycin in animals and man with reference to its clinical trial, Ann. New York Acad. Sc. 53:242, (Sept. 15) 1950.
5. Welch, H.: Absorption, excretion and distribution of terramycin, Ann. New York Acad. Sc. 53:253, (Sept. 15) 1950.
6. Sayer, R. J.; Michel, J. C.; Moll, F. C., and Kirby, W. M. M.: Terramycin: Clinical, pharmacologic, and bacteriologic studies, Am. J. M. Sc. 221:256, (March) 1951.
7. Michel, J. C.; Sayer, R. J., and Kirby, W. M. M.: Effect of food and antacids on blood levels of aureomycin and terramycin, J. Lab. & Clin. Med. 36:632, (Oct.) 1950.
8. Parsons, W. B., and Wellman, W. E.: Use of antacids to control nausea and vomiting caused by terramycin, Proc. Staff Meet., Mayo Clin. 26:260, (July 4) 1951.
9. Werner, C. A.; Knight, V., and McDermott, W.: Absorption and excretion of terramycin in humans: Comparison with aureomycin and chloramphenicol, Proc. Soc. Exper. Biol. & Med. 74:261, (June) 1950.
10. Caldwell, Jr., E. R.; Spies, H. W.; Wolfe, C. K.; Lepper, M. H., and Dowling, H. F.: Treatment of various infections with terramycin, J. Lab. & Clin. Med. 36:747, (Nov.) 1950.
11. Finland, M.; Gocke, T. M.; Jackson, G. G.; Womack, C. R., and Kass, E. H.: Clinical studies on terramycin, Ann. New York Acad. Sc. 53:290, (Sept. 15) 1950.
12. Pulaski, E. J.: Place of antibiotics in field of surgery, Ann. New York Acad. Sc. 53:347, (Sept. 15) 1950.
13. Poole, M. J.: Personal communication.

GENERAL PRACTICE CLINICS

14. *The Use of Myanesin (Tolserol) in Black Widow Spider Bite.* MILTON ENDE AND W. YOUNGBLOOD, Petersburg, Va. Virginia M. Monthly *80*:24–5, January 1953.

Since tolserol relaxes muscle spasm, which appears to be the fundamental difficulty in black widow spider bite, it was felt that this drug might be of value in the treatment of arachnidism. A review of other medications used in the treatment of this condition were included. One patient was given tolserol intravenously with marked relief while the drug was being injected. 7 references.—*Author's abstract.*

15. *A Complicated Case of Primary Hyperthyroidism.* ELMER C. BARTELS AND GORDON L. ROSS, Boston, Mass. Lahey Clin. Bull. *8*:36–8, October 1952.

An unusual case is presented of primary hyperthyroidism and associated hypertensive heart disease with auricular fibrillation and congestive heart failure. This case demonstrates some of the complications that can arise in the preoperative medical management of this disease.

The complications include slow initial response to medical treatment (propylthiouracil) and dramatic response to tapazole to the point where myxedema developed and responded to desiccated thyroid. Cardiac arrest occurred during induction of anesthesia, which led to cerebral anoxemia with disturbed cerebration for two weeks. The patient recovered completely.—*Elmer C. Bartels, M.D.*

16. *Varicella Pneumonia.* SAMUEL SASLAW, JOHN A. PRIOR, AND BRUCE K. WISEMAN, Columbus, Ohio. Arch. Int. Med. *91*:35–42, January 1953.

A severe virus type pneumonia with extensive bilateral nodular pulmonary infiltrates was observed in 3 adults with chicken pox. The paucity of physical findings in the lungs was in distinct contrast to the extensive infiltration seen in x-rays. All 3 patients showed rapid and dramatic clinical improvement. The clearing of the lung fields paralleled the improvement of skin lesions. Sputum examinations were not consistent with bacterial pneumonia; blood cultures were negative. Leukocyte counts were only moderately elevated in 2 and not affected in one. Serial serologic studies for primary atypical pneumonia, psittacosis and Q fever were negative. The marked similarity in the clinical and radiologic findings in all 3 patients was striking. No specific effect was attributed to either penicillin or aureomycin. Since a review of autopsies of fatal cases of chicken pox has shown visceral involvement, these 3 cases in all probability represented varicella pneumonia. 3 references. 7 figures.—*Author's abstract.*

Quarterly Review of OPHTHALMOLOGY

Editorial Board

CONRAD BERENS, M.D.
Editor-in-chief

national board

WALTER S. ATKINSON, M.D.
Watertown, N. Y.

ROBERT E. BANNON, D.O.S.
Southbridge, Mass.

WILLIAM L. BENEDICT
Mayo Clinic

EUGENE M. BLAKE, M.D.
Yale University

HENRY N. BRONK
New York, N. Y.

JOHN W. BURKE, M.D.
Washington, D. C.

BURTON CHANCE, M.D.
Philadelphia, Pa.

DAVID G. COGAN, M.D.
Harvard University

FREDERICK C. CORDES, M.D.
University of California

ALFRED COWAN, M.D.
University of Pennsylvania

C. L. CROUCH
New York, N. Y.

PERCE DELONG, M.D.
University of Pennsylvania

EDWIN B. DUNPHY, M.D.
Harvard University

F. BRUCE FRALICK, M.D.
University of Michigan

GLEN FRY, O.D.
Ohio University

EVERETT L. GOAR, M.D.
Houston, Texas

JAMES N. GREEAR, M.D.
Georgetown University

JACK S. GUYTON, M.D.
Johns Hopkins University

PARKER HEATH, M.D.
Winchester, Mass.

S. RODMAN IRVINE, M.D.
University of Southern California

DANIEL B. KIRBY, M.D.
New York University

ARLINGTON C. KRAUSE, M.D.
Chicago, Ill.

ALBERT N. LEMOINE, M.D.
Kansas City, Mo.

MICHEL LOUTFALLAH, M.D.
Santa Barbara, Calif.

DONALD J. LYLE, M.D.
University of Cincinnati

JULIUS NEUMUELLER, O.D.
Haddonfield, N. J.

CECIL S. O'BRIEN, M.D.
Tucson, Arizona

BRITAIN F. PAYNE, M.D.
New York University Medical College

OGDEN D. PINKERTON, M.D.
Honolulu, T. H.

LAWRENCE T. POST, M.D.
Washington University, St. Louis, Mo.

AVERY D. PRANGEN, M.D.
Mayo Foundation

ALGERNON B. REESE, M.D.
Columbia University

C. WILBUR RUCKER, M.D.
Mayo Foundation

ALBERT D. RUEDEMANN, M.D.
Wayne University

G. VICTOR SIMPSON, M.D.
Washington, D. C.

K. B. STODDARD, PH.D
University of California

GEORGIANA DVORAK-THEOBALD, M.D.
Chicago, Ill.

PHILLIPS THYGESON, M.D.
San Jose, Calif.

CLIFFORD L. TRELEAVEN, A.M.
Columbia University

DERRICK VAIL, M.D.
Northwestern University

ROBERT T. WONG, M.D.
Honolulu, T. H.

JOSHUA ZUCKERMAN, M.D.
New York University

international board

MOACYR EYCK ALVARO, M.D.
Sao Paulo Medical College
Sao Paulo, Brazil

MARC AMSLER, M.D.
Universitates-Augenklinik
Zurich, Switzerland

J. RINGLAND ANDERSON, M.D.
Melbourne, Australia

RAUL ARGANARAZ, M.D.
Buenos Aires, Argentina

ALFREDO ARRUGA, M.D.
Barcelona, Spain

L. E. BARRERE, M.D.
Lima, Peru

ALBERTO VAZQUEZ BARRIERE, M.D.
Montevideo, Uruguay

RODRIGUEZ BARRIOS, M.D.
Montevideo, Uruguay

M. SOBHY BEY, M.D.
Cairo, Egypt

GIAMBATTISTA BIETTI, M.D.
Parma, Italy

LUIS SANCHEZ BULNES, M.D.
Mexico, D. F.

HOWARD COVERDALE, M.D.
Auckland, New Zealand

SIR STEWART DUKE-ELDER, M.D.
London, England

J. M. ESPINO, M.D.
Caracas, Venezuela

STEPHEN DE GROSZ, M.D.
Budapest, Hungary

A. HAGEDOORN
Universiteit van Amsterdam,
Holland

EDWARD HARTMANN, M.D.
Paris, France

RAFAEL IRRIBARREN, M.D.
Buenos Aires, Argentina

ALEXANDER JOKL, M.D.
Johannesburg, South Africa

KARL LINDNER, M.D.
Vienna, Austria

T. H. LUO, M.D.
Peiping, China

CLEMENT MCCULLOCH, M.D.
University of Toronto

JORGE MALBRAN, M.D.
Buenos Aires, Argentina

EDGARDO MANZITTI, M.D.
Buenos Aires, Argentina

HENRIQUE MOUTINHO, M.D.
Lisbon, Portugal

J. V. V. NICHOLLS, M.D.
McGill University Medical School
Montreal

R. PACHECO-LUNA, M.D.
Guatemala City, Guatemala

L. B. SOMERVILLE-LARGE, M.D.
Dublin, Ireland

KARL WESSLEY, M.D.
Munich, Germany

TOMAS R. YANEZ, M.D.
University of Havana

INCORPORATING INTERNATIONAL RECORD OF OPHTHALMOLOGY

FOREWORD

The objective of the QUARTERLY REVIEW OF OPHTHALMOLOGY is to bring together in one publication concise but authoritative abstracts of current articles on ophthalmology, according to an all inclusive plan which will include all special, state, and national journals as well as the bulletins of clinics, hospitals, etc., and the transactions of meetings. This embraces both the domestic and foreign literature.

To assist the reader to locate quickly the articles of current interest all data are classified and published according to the following systematic plan:

Anatomy, Embryology, Heredity, Development and Nutrition

Optics, Physiology and Psychology of Vision

Physiology, Chemistry and Biochemistry of the Eye

Pathology, Bacteriology and Immunology

Diagnostic Methods of Examination Biomicroscopy and Photography

Ocular Movements and Motor Anomalies, Nystagmus, Reading Disability

Anomalies of Refraction and Accommodation, Contact Lenses

Conjunctiva

Cornea, Sclera and Tenon's Capsule

Anterior Chamber and Pupil

Uveal Tract and Sympathetic Ophthalmitis

Crystalline Lens

Vitreous Humor

Retina

Neuro-Ophthalmology, Optic Nerve, Visual Pathways, Centers and Visual Fields

Eyeballs, Exophthalmos and Enophthalmos

Glaucoma and Hypotony

Lacrimal Apparatus

Eyelids

Orbit

Allergy

Anesthesia

Medical Ophthalmology

Pharmacology, Toxicology and Therapeutics

Comparative Ophthalmology

Tropical Ophthalmology

Hygiene, Prophylaxis, Occupational Ophthalmology and Injuries

Illumination and Illuminating Engineering

Ophthalmic Sociology

Education, History and Institutions

Miscellaneous

Book Reviews

Announcements

A section entitled International Record of Ophthalmology is included at the beginning of the journal. The Record Section consists of advanced clinical and experimental reports.

RARER THAN A PLATYPUS...

is the surface anesthetic that can compare with Pontocaine hydrochloride for dependability, durable effect and penetrating power.

For a great variety of therapeutic and surgical procedures on the pharynx, larynx, trachea, bronchi and the eye, you can rely upon prolonged and penetrating Pontocaine.

Effective in anesthetizing mucous membranes of the pharynx, larynx, trachea, bronchi and the eye.

PONTOCAINE®
HYDROCHLORIDE

Winthrop-Stearns Inc.
New York 18, N. Y. • Windsor, Ont.

Supplied

for surface anesthesia *in ophthalmology* . . . as 0.5 per cent solution in bottles of ½ oz. and 2 oz., and 0.5 per cent ointment in ⅛ oz. tubes.
for surface anesthesia *in rhinology* . . . as 2 per cent solution in bottles of 1 oz. and 4 oz.

For 5 hour nerve block and infiltration anesthesia

surgical, diagnostic and therapeutic 0.15 per cent solution, vials of 100 cc.

Pontocaine (brand of tetracaine) trademark reg. U.S. & Canada

Quarterly Review of **OPHTHALMOLOGY**

ABSTRACTS

OPTICS, PHYSIOLOGY AND PSYCHOLOGY OF VISION

18. *Maximum Electrical Response of the Human Retina on Stimulation with Monochromatic Light of Various Wave Lengths.* H. E. HENKES AND P. B. ROTTIER. Ophthalmologica. *125*:32–42, January 1953.

In the experiments a strictly monochromatic light was used for stimulation of the retina, the response being measured by electroretinography by the method developed by Karpe. In these experiments dark adaptation was determined for one hour before the light stimulation of the retina, and there were intervals of several minutes between the flashes of light employed to maintain the retina in a good dark-adapted state. With monochromatic light ranging in wave length from 340 mμ to 1014 mμ, a maximum b-potential was obtained in the electroretinograph of 0.55 to 0.60 m.V with wave lengths 365 to 380 mμ. These results were obtained in persons who under clinical conditions showed a maximum electroretinographic response of approximately 0.35 m.V. The state of dark adaptation is evidently of importance in such retinal responses; as is also the metabolic condition of the nerve elements of the retina. 7 references. 4 figures.

19. *Luminance Thresholds for the Resolution of Visual Detail During Dark Adaptation.* J. L. BROWN, C. H. GRAHAM, H. LEIBOWITZ, AND H. B. RANKEN, New York, N. Y. J. Optic. Soc. America. *43*:197, March 1953.

Luminance thresholds for the visual resolution of various widths of alternating light and dark lines were determined at various times during dark adaptation. The finest gratings, representing high degrees of visual acuity, show only a single cone curve that drops from a high luminance threshold during the first moments of dark adaptation to a final steady level that is reached after about 7 to 10 minutes in the dark. Coarse gratings produce a duplex curve that shows an initial cone portion and a delayed rod portion. Visual acuity is a parameter that sets the position of a given curve on the log threshold axis. The higher the degree of resolution required, the higher the dark adaptation threshold. At a constant

grating luminance, visual acuity rises rapidly to a maximum during dark adaptation; the higher the luminance, the earlier and more rapid the rise, and the higher the maximum. Visual acuity increases at all dark adaptation times with increase in luminance.

DIAGNOSTIC METHODS OF EXAMINATION, BIOMICROSCOPY AND PHOTOGRAPHY

20. *Some Contributions to the Clinical Application of Electroretinography.* GEORGE W. BOUNDS, JR. AND BRUNO BAGOLINI. Abstract of paper read at the Fifth Annual Meeting of the Midwestern Section, Association for Research in Ophthalmology, St. Louis, March 27, 1953.

This paper briefly discusses the main features and components of the electroretinogram. The average values of the light and dark adapted electroretinogram, as described by Karpe, are presented. The authors have employed a high intensity stroboscopic light, and with this method are able to obtain a- and b-waves in the light and dark adapted states. The interpretation of the double peaked positive component is discussed. We feel the first portion is due to the cone mechanism, and the second to the rod mechanism. Four pathologic cases are presented in which we feel that the electroretinogram has aided us either in the diagnosis or treatment of the case.—*Author's abstract.*

21. *Memory Aid for the Parallax Test.* J. I. PASCAL. American J. Ophth. *36*:262–63, February 1953.

The subjective counterpart of the prism-cover test for heterophoria is the so-called parallax test. Here the patient observes a shift of the object fixed, in cases of heterophoria, as the card is moved from one eye to the other. The type of heterophoria thus disclosed is easily ascertained if one remembers that both eyes move as the target seems to move. The movement behind the cover tells the kind of heterophoria.—*Author's abstract.*

22. *The Truth About "False" Torsion.* J. I. PASCAL. Ophthalmologica. *125*:190–96, March 1953.

True torsion is a wheel-like rotation of the eye on an anteroposterior axis. This axis runs practically from the fovea in the back of the eye to the midpoint of the cornea in front. In this rotation the meridians of the cornea rotate in exactly the same direction as the meridians of the retina. In extorsion, for example, the upper end of the vertical meridian of the cornea, as well as the upper end of the vertical meridian of the retina, is rotated outwards.

False torsion is not a wheel-like movement. It is an inclination of the corneal and retinal meridians as an accompaniment of a movement of the eye on an oblique axis in Listing's plane. Listing's plane is a transverse coronal plane passing through the equator of the eye when the latter is in the primary position. An axis in

Listing's plane can have no component in an axis running anteroposteriorly. A rotation of the eye on an axis in Listing's plane produces opposite displacements of everything on the anterior half of the eye as compared to the corresponding structure on the posterior half of the eye. Thus in false torsion the meridians of the cornea and of the retina are inclined in opposite directions.

In designating duction movements, in-out, up, or down, we use the anterior pole of the cornea as the point of reference. In designating true torsion we can use the meridians of the cornea or the meridians of the retina as a basis, since they both rotate in the same direction. But in designating false torsion, in order to continue with our standard and well-ingrained terminology, we must use as a reference frame the retinal meridians. These, in false torsion, rotate opposite to the corneal meridians. For the sake of uniformity it is best to refer to all torsion movements with reference to the inclination of the retinal meridians. The Pascal muscle schema by eliminating any indication of a rotary eye movement in false torsion lends itself especially well for the correct analysis of all eye movements. 6 references. 2 figures.—*Author's abstract.*

OCULAR MOVEMENTS AND MOTOR ANOMALIES, NYSTAGMUS, READING DISABILITY

23. *The Two Phases of Abnormal Retinal Correspondence.* J. I. PASCAL. Am. J. Ophth. *35*:August, 1952.

Normal and abnormal retinal correspondence have two different phases which must be clearly differentiated. One involves the presence of bimacular superposition or separation, i.e., whether or not the two maculae have the same visual direction or not. The other involves the presence of macular comacular separation or superposition, i.e., whether noncorresponding areas have different or the same visual direction. 1 reference.—*Author's abstract.*

ANOMALIES OF REFRACTION AND ACCOMMODATION, CONTACT LENSES

24. *How a Correcting Lens Changes the Length of the Eye.* J. I. PASCAL. Eye, Ear, Nose and Throat Monthly. *32*:146–48, March 1953.

The effect of a correcting lens on an ametropic eye is not to change the refractive power of the eye, but to change its optical length. The optical length of an eye is the distance from P_2 (the second principal point) to F_2 (the second principal focus). The hyperopic eye is an eye which is too short for its refractive power, the plus lens by moving P_2 forward lengthens it sufficiently for its power. The myopic eye is an eye which is too long for its refractive power, the minus lens by moving P_2 backward shortens it sufficiently to correspond to its power.

As far as the total power of lens and eye is concerned, both the plus and minus lens may cause an increase of the total power, a decrease of the total power, or

leave the power unchanged. A lens placed before an emmetropic eye changes the optical length of the eye. A plus lens moves P_2 forward, thus lengthening the eye and making it myopic. A minus lens moves P_2 backward, thus shortening the eye and making it hyperopic.—*Author's abstract.*

25. *Effect of Accommodation on the Retinal Image.* J. I. PASCAL. Brit. J. Ophth. *36*:676–78. 1952.

The effect of accommodation on the size of the retinal image is given by some authors as an increase in size during accommodation and by others as a decrease in size during accommodation. One reason for this apparent contradiction is that the first group of authors refers to the retinal image, and the second group to the optical image; but both statements are incomplete in that there is no reference to the images compared. Several such comparisons are here discussed as well as the special significance of the retinal image. The most logical comparison is that made between the clear retinal image of a distant object subtending a given angle, and the clear retinal image of a near object subtending the same angle, for which the eye accommodates. In this way it may be shown that the retinal image during accommodation is larger than the retinal image during nonaccommodation.—*Author's abstract.*

26. *Lens Replacement of Accommodative Activity.* J. I. PASCAL. Ophthalmologica. *123*:391–96, June 1952.

In figuring the power of the plus lens, which would replace some or all of the accommodative activity necessary for a given distance by a natural emmetrope, the usual method employed is much too approximate. By the simple formula $L' \frac{A}{1 - dA}$ which gives the lens equivalent for the accommodation used, it is possible to obtain the correct answer with a minimum of work. For the corrected ametrope the accommodative unit "U" must be used in the calculations, and the formula becomes $L' \frac{A}{U - dA}$.

27. *Clinical Observations in Myopia and Techniques for Myopia Control.* WILLIAM SMITH. Optical J. & Rev. Opt. *90*:10, April 1953.

The author states that not all myopes respond to visual training and that results from training are not lasting and must be repeated periodically. Visual training in functional myopia, unlike treatment procedures for most other types of anomalies of the visual apparatus, has limitations in extensiveness and scope.

CORNEA, SCLERA AND TENON'S CAPSULE

28. *Changes in Corneal Tissue during Conservation and Their Probable Effect on the Postoperative Course of Corneal Transplantation (Les modifications du tissu cornéen pendant la conservation et leur probable influence sur le cours post-opératoire de la kératoplastie).* F. ORZALESI AND P. CIUFFO, Cagliari, Italy. Ophthalmologica. *125*:21–31; 91–111, January and February 1953.

After a review of the literature on methods of preservation of corneal tissue to be used as grafts and the various theories in regard to the failure of the graft due to its becoming opaque, the authors report their own studies of the effect of different methods of preservation on corneal tissues. Using Menkin's methods, they found that the extracts of corneal tissues contain substances that increase capillary permeability and cause an exudation of leukocytes. While these substances are not histamine, they act in the same way. In animal experiments it was found that the use of cortisone tended to counteract these effects on corneal tissue extracts. From these findings they conclude that when the corneal graft becomes opaque, it is due to an allergic reaction between the host and the graft. 55 references. 4 figures.

ANTERIOR CHAMBER AND PUPIL

29. *Iridectomy for Drawn-up Pupil.* PAUL A. CHANDLER, Boston, Mass. Abstract of a paper given at the Post Testimonial Program, Washington University School of Medicine, March 28, 1953.

Keratome incision is begun in clear cornea, just above the limbus below. The incision is made in a slanting fashion so that the tip enters the anterior chamber 3 or 4 mm. beyond the point of engagement. At the entrance of the anterior chamber, the incision should be about 4 mm. broad. The iris is grasped with smooth forceps, pulled out, and a small piece excised. The anterior chamber is reformed with air, and no suture is required.

The operation is designed for cases of drawn-up pupil where the lens is present, but it is also applicable to cases of drawn-up pupil in aphakic eyes if the extraction has been intracapsular and there is no reason to anticipate a membrane behind the iris.—*Author's abstract.*

UVEAL TRACT AND SYMPATHETIC OPHTHALMITIS

30. *The Vogt-Koyanagi Syndrome (Das Vogt-Koyanagische Syndrom).* Z. AGG, University of Pécs, Hungary. Ophthalmologica. *125*:43–51, January 1953.

The clinical symptoms of the Vogt-Koyanagi syndrome are bilateral uveitis not due to trauma, vitiligo, prematurely gray hair, alopecia, or deafness. In the author's case the patient was a man thirty-six years of age who noted a marked diminution of vision four days after a severe headache. Papillo-chorioretinitis in

this case was associated with iritis, which was at first slight, but resulted in the production of synechia. There was vitiligo involving the skin of the eyelids and premature graying of the hair. The state of the patient's hearing was not determined. As there was a history of cervical lymphoma in childhood and of recurrent osteomyelitis, the possibility of a chronic tuberculosis as the cause of the disease was considered; a trial of streptomycin therapy, on the basis of this assumption, resulted in definite improvement. 13 references. 3 figures.

31. *Multiple Malignant Melanomas in One Eye.* DAVID A. ROSEN AND GARDNER S. MOULTON. Trans. Am. Acad. Ophth. *57*:107, Jan.-Feb. 1953; Amer. J. Ophth. *36*:73, January 1953.

There have been very few cases of multiple primary malignant melanomas of the choroid. A critical review of the cases reported by Fuchs, Rochat, and Velhagen revealed that none of the instances fulfilled rigid criteria for multiple tumors in one eye. Serial sections were not made in any of the cases in the literature.

The case reported is of a 52 year old white male who was first noted to have a lesion in his left eye in 1947. He sought medical attention four years later, at which time he was seen to have a large dark mass extending out from the macula to the far periphery, and a detachment of the whole temporal half of the retina. Physical examination revealed no evidence of other primary tumors or of metastases.

The globe was enucleated. Gross examination of the globe revealed that, in addition to the large mass noted ophthalmoscopically, there were four discreet elevated lesions in the choroid. Microscopic examination revealed a separate malignant melanoma of the ciliary body. Serial sections through one of the smaller choroidal lesions revealed two entirely independent melanomata. Furthermore, a benign melanoma of the choroid was found. There was a varying cytology in the separate lesions, ranging from spindle cell type B through epithelioid cell and mixed cell portions.

This case is felt to be one of multiple primary malignant melanomas in one eye. Against the possibility of this being an instance of multiple metastases to the uvea is the fact that none of the lesions are in relationship with or appear to arise from blood vessels. Moreover, the pathologic findings are identical to those of ordinary malignant melanomas of the uveal tract. Finally, the patient presented no evidence of other primary tumor or of metastases elsewhere.

CRYSTALLINE LENS

32. *Modern Trends in Cataract Surgery.* THURBER LE WIN. Abstract of a paper given at the 1953 Annual Convention, Medical Society of the State of New York, Buffalo, N. Y., May 4–8th.

In discussing modern trends in cataract surgery, it must be acknowledged that marked advances have been made in the past few years. The newer concepts of the role played by the Zonular membrane have been emphasized by Derrick Vail

in the Bedell Lecture at the Wills Hospital last year, by Minsky in his outline at the Instruction Section at the Academy meeting, and by Kirby in his recent publication. These men have all called attention to the fact that the Zonular membrane is truly a membrane and not merely a group of fibers as some histologists have claimed. How this concept ties in with recent procedures is explained.

The increased use of the erisophake and some recent improvements in the instrument and technics are described. Improvements in suturing cataracts wounds with some authors advocating mattress sutures is noted. The Ridley operation, in which Warren Reese has been a pioneer in this country, may be more than a fad and its possibilities are of great interest.

RETINA

33. *The Early Physical Signs in the Retina Seen in Essential Hypertension.* HENRY MINSKY, New York, N. Y. Abstract of a paper given at Pan-American Medical Association Eighth International Cruise-Congress, January, 1953.

When a case of essential hypertension has advanced to the stage where there are hemorrhages and exudates in addition to vascular changes in the fundus, it is a relatively simple matter for the clinician to appraise the severity of his patient's disease. It is in the early stages of hypertension, however, where it would be even more valuable for the physician to be able to recognize the fact that his patient has already established the hypertensive status, even though he is in a period of remission. To be able to do so, he must learn to attach sufficient importance to certain concurrent physical signs in the fundus when the disease is first established. In such an early diagnosis lies the hope of preventive medicine with emphasis on instituting a proper management in what from past experience promises to become a chronic, worsening progressive disease, which ultimately will compromise health and threaten life.

Long before a hemorrhage or an exudate appears, the changes in the arterioles have taken place. Probably, the first unequivocal sign to show itself is a narrowing in a portion of one or more arterioles near the disc margin. The sequence of further changes causes more and more alterations in the caliber of the arteriolar tree and results in physical signs signifying greater involvement of the general circulation and indicates a steady march of progressively deteriorating impacts upon the individual.

The definitive signs of established hypertension of the general circulation that are seen in the retina are: (1) uniform narrowing; (2) localized narrowing in an otherwise unnarrowed arteriole; (3) distal tapering: normal at the beginning, narrowed peripherally; (4) proximal tapering: narrowed proximally, normal calibre beyond; (5) disproportionate branching: one branch narrowed, the other normal; (6) distally tapered fork: stem normal, both branches narrowed; (7) proximally tapered fork; stem narrowed, branches normal; (8) similar changes in the branches of the second, third, and fourth order; (9) diseased arterio-venous crossing—(a) concealment, (b) displacement: anterior, posterior, lateral, and (c) banking; (10) retinopathy.—*Author's abstract.*

NEURO-OPHTHALMOLOGY, OPTIC NERVE, VISUAL PATHWAYS, CENTERS AND VISUAL FIELDS

34. *Infectious Mononucleosis with Diffuse Involvement of the Nervous System.* MARTIN J. FREEMAN, LAWRENCE T. ODLAND, AND EDWARD A. CLIVE. Arch. Neurol. & Psychiat. *69*:49, January 1953.

A case is reported in which the chief symptoms were those of central nervous system involvement; the electroencephalogram showed changes typical of encephalitis. The cerebrospinal fluid showed 25 lymphocytes per cc.; and the Paul-Bunnell quantitative heterophile agglutination test of the cerebrospinal fluid was positive—the first case reported in which this test has been made on the spinal fluid. The patient made an uncomplicated recovery. This patient had two episodes of twitching of the left side of the face and deviation of the eyes to the left. In a review of the literature, it was found that involvement of the central nervous system in infectious mononucleosis shows varying clinical symptoms; the unusual signs noted in such cases include ptosis, papilloretinal edema, and ocular paralyses. In any obscure infection of the central nervous system, the possibility of infectious mononucleosis should be considered. 11 references. 2 figures.

35. *Traumatic Cranial Injuries. Neurosurgical Diagnosis and Treatment.* JUAN NEGRIN, JR., New York, N. Y. Abstract of paper presented at the Eighth Congress of Pan-American Medical Association Cruise, January 1953.

After preliminary remarks on head injuries accompanied by traumatic lesions in other parts of the body (chest, abdomen, extremities), a detailed discussion on simple cranial injuries was presented.

The problems of cerebral concussion and more severe lesions were discussed. A detailed history with special reference to changes in alertness, depth of consciousness, and intermittent periods of drowsiness is of primary importance in arriving at a proper diagnosis of the head injury or combination of injuries present. A meticulous neurologic examination is also most necessary. Emphasis was placed on the diagnostic value of ocular findings in acute head injuries. A dilated pupil is present, most of the time, on the same side of an epidural or subdural hematoma, with a lineal fracture of the skull on the same side of the dilated pupil in epidural hematomas, and on the opposite side in subdural hematomas. The epidural hematomas require the most urgent surgical removal in order to avoid the patient's death within hours from the head injury. Very often the only localizing and definite diagnostic sign is the presence of a dilated pupil, hence, the vital importance of this ocular finding. In fractures of the anterior fossa of the base of the skull, x-rays are often negative, and periocular ecchymosis, sometimes appearing days after the accident, are the only signs indicative of the severity of trauma sustained and of the exact location of the fracture in the base of the skull.

Choked disc or papilloedema practically are never found in acute head injuries. They are most unusual in subchronic cases and very rare in chronic traumatic head injuries.

The diagnostic value of x-rays, lumbar puncture, electroencephalography, air studies (pneumo- and ventriculograms) and cerebral angiography were discussed, and each subject was illustrated with lantern slides of clinical cases. The surgical treatments of simple scalp lacerations, depressed skull fractures and intracranial hematomas, and the importance of neurologic and ocular findings in their management were outlined.

The closing remarks were directed towards post-traumatic sequelae, such as epilepsy, psychoneurosis, ophthalmoplegias and exophthalmus, which may result from retrobulbar hematoma from fractures around the optic foramen or cavernous sinus thrombosis or arteriovenous fistula in the region of the cavernous sinus.—*Author's abstract.*

36. *The Optic Chiasm.* D. PARKINSON. Canad. M. A. J. *68*:172, February 1953.

This is a historical note on the discussions between Dr. W. Briggs and Sir Isaac Newton on the decussation of the optic nerves at the chiasm. 1 reference.

37. *Visual Field Studies in Neurosurgical Problems.* MAX CHAMLIN, New York, N. Y. Eye, Ear, Nose and Throat Monthly *31*:415–22, August 1952.

The author discusses the following six types of diagnostic problems that the neurologist and neurosurgeon encounter and call upon the ophthalmologist to answer: (1) Presence or absence of papilledema; (2) differential diagnosis of papilledema; (3) presence or absence of optic atrophy and its cause; (4) differential diagnosis between optic neuritis and an intracranial mass lesion causing loss of vision; (5) presence or absence of chiasmal interference and its cause; (6) presence or absence of homonymous hemianopia and site of interference.

1. In discussing the *presence or absence of papilledema*, the author emphasizes particularly the size of the blind spot. He stresses the importance of measuring the blind spot carefully and doing minimal measurements, such as a 2/2000 white test. With a visual angle as small as this, most normal people have a pericecal zone of partial amblyopia which measures no more than 1° all around the blind spot. Enlargement beyond this pericecal zone must be considered as abnormal if there is nothing in the fundus to account for such enlargement. Therefore, if a disc looks suspicious of papilledema, enlargement beyond this pericecal zone with minimal testing must be considered as indicative of early papilledema. He stresses the importance of avoiding angioscotomas at the upper and lower edges of the blind spot, and thus avoiding a false enlargement of the blind spot in the vertical meridians.

2. *Differential diagnosis of papilledema.* The conditions most commonly confused with papilledema are optic neuritis, pseudopapilledema or pseudoneuritis, and drusen of the optic nerve head. The important differential diagnosis between optic neuritis and papilledema is that in optic neuritis there is usually an acute loss of vision which occurs quite suddenly. It is usually unilateral and the visual field defect is most frequently a cecocentral scotoma or a paracentral scotoma in

the form of a nerve fiber bundle defect. Occasionally, there is a defect which reaches out to the periphery and this may cause some confusion. In papilledema, on the other hand, the most important point is that the field shows an enlargement of the blind spot with relatively little or slow involvement of the central area, if at all, and this occurs only after a long period of time. There is no sudden acute episode of marked loss of vision. Furthermore, it is usually bilateral rather than unilateral. The most important point is that the visual fields are so completely different in the two conditions that if other factors are confusing, central field studies should make the differential quite definite. As for pseudopapilledema or pseudoneuritis, this is a congenital type of anomalous formation of the optic disc in which there is a heaping up of excess glial tissue with blurring of the disc margins, and absence of physiologic cup. The important point is that in these cases the blind spot is always normal and there are no peripheral defects. In so-called drusen of the optic nerve head, there is an accumulation of hyalin tissue, very often with the formation of rounded concretions known as "drusen." If these are visible, then the diagnosis is quite evident. If they are buried below the surface of the papilla, the ophthalmoscopic picture may be very similar to that of papilledema. Furthermore, the blind spot is enlarged in cases of drusen of the optic nerve head, and this causes even more confusion. Occasionally, rather specific types of field defects are found with drusen, and these may help in the differential diagnosis. Often the case must be studied from the point of view of the history and other clinical findings before a definite differential diagnosis between papilledema and drusen of the optic nerve head can be made. At times, it is necessary to follow such cases for a while before making up one's mind as to which condition he is dealing with.

Other conditions likely to be confused with papilledema but much less difficult to differentiate are medullated nerve fibers, chorioretinitis juxtapapillaris, hypertensive neuroretinopathy, peripapillary changes of myopia and arteriosclerosis and thrombosis of the central retinal vein.

3. *Optic atrophy.* The presence or absence of optic atrophy is frequently difficult to decide by the appearance of the disc alone. What appears pale to one observer may appear normal to another. The author has found that the most reliable means of evaluating whether or not a disc is atrophic is to do a functional test in the form of a complete visual field study. In other words, the entire field of vision must be tested. Thus, the periphery must be tested with a 3/330 white and a 1/330 white for minimal defects and the more central portion of the field with a 1/2000 white and a 0.5/2000 white or 5/2000 red for the inner isopters. The blind spots must be studied with 2/2000 white. Minimal technics, such as described by the authors in previous articles, must be employed. If, with these tests, there are no field defects found, one may assume that what looks like optic atrophy is really a physiologic type of pallor. If, on the other hand, visual field defects are found, the pale-looking disc may be considered as an atrophic one, and the type of field defect, together with the history of the case, should help to establish the cause of the optic atrophy.

4. *Differential diagnosis between optic neuritis and an intracranial mass lesion*

causing the loss of vision. Here, the author stresses the importance of a very thorough history, remembering that in inflammatory lesions, the loss of vision is usually quite sudden, while in intracranial mass lesions, pressing on the optic nerves, the loss of vision is usually a rather slow one. Furthermore, he stresses the importance of the peripheral defect preceding the central involvement in mass lesions, and the importance of finding an early temporal defect in the contralateral eye as indicative of a mass lesion. In optic neuritis, on the other hand, the field defect is most apt to be a cecocentral one, although occasionally there are nerve fiber bundle defects which may break through to the periphery and thus resemble the interference due to mass lesions. Differential diagnosis of these conditions is discussed.

5. *Chiasmal interference.* The typical defects of chiasmal interference are those of bitemporal hemianopia when these defects are detected with the 1 mm. test object at 2000 mm. Most important are the purely hemianopic features which are characteristic of a mass lesion at the chiasm. Inflammatory lesions of this area are so uncommon compared to mass lesions that if truly hemianopic features are found, that is, truly vertical dividing lines between nasal and temporal defect, one must consider these lesions as due to mass rather than inflammation, until proved otherwise. The importance of finding an early upper temporal defect in the contralateral eye, especially with the 1/2000 white, is stressed as an important factor in diagnosing a mass lesion near the chiasm.

6. *Homonymous hemianopia.* The author stresses the importance of finding a homonymous defect in those cases where the neurosurgeon is looking for so-called "sidedness" of a lesion. Furthermore, in cases where the so-called sidedness of a cerebral lesion is known, the presence or absence of a field defect may help the surgeon to determine whether the lesion is higher up or lower down in the cerebrum. Definite incongruity is quite characteristic of subgeniculate lesions, and congruity more apt to be associated with supergeniculate lesions. Macular splitting is practically always subgeniculate, while macular sparing may be either subgeniculate or supergeniculate in origin. The author stresses the importance of using minimal types of tests and gives references in the literature to such minimal types of testing for early homonymous hemianopic defects. 6 references. 9 figures.—*Author's abstract.*

EYEBALLS, EXOPHTHALMOS AND ENOPHTHALMOS

38. *Evisceration with Plastic Intrascleral Implants.* C. BERENS AND F. A. ROSA, New York, N. Y. Am. J. Ophth. *36*:356, March 1953.

The authors introduce a Rosa hollow plastic intrascleral implant which is spherical on its posterior half and with a flattened anterior surface, which they claim affords better motility of a prosthesis following evisceration. The technic of evisceration includes a circumcorneal conjunctival incision followed by a scleral section which includes one half of the circumference of the eyeball made with a

narrow cataract or curved glaucoma knife. The scleral section is completed with curved scissors. Wedge-shaped pieces of sclera are excised with scissors at the ends of the horizontal diameter of the sclera wound to facilitate good closure. The contents of the eye is eviscerated with an evisceration spoon. Hemostasis is obtained with compression from a plastic compressor. From four to six special double-armed braided black nylon sutures are inserted through the edge of the scleral lips. The implant is placed in the scleral cavity and the sutures tied. The conjunctiva is closed with a running plain catgut suture which is locked in the center and at the extremities of the wound.

The technic is simple and surgically less traumatic than enucleation, causing less atrophy of the orbital tissue and less sinking of the upper eyelid. Evisceration is preferable to enucleation as a means of obviating the danger of meningitis from cutting the optic nerve in the presence of a purulent infection.

The authors maintain that sympathetic ophthalmia does not follow evisceration more often than enucleation, and suggest that the procedure be employed in preference to enucleation whenever indicated.

GLAUCOMA AND HYPOTONY

39. *Aqueous Outflow Measurements by Continuous Tonometry in Some Unusual Forms of Glaucoma.* BERNARD J. MANSHEIM, Iowa City, Iowa. Abstract of a paper given at The Fifth Annual Meeting, Midwestern Section, The Association for Research in Ophthalmology, March 27, 1953.

The principle and technic of tonography are described, and the average figures for the coefficient of facility of aqueous outflow and for the net rate of aqueous formation are given for normal eyes and for eyes with glaucoma.

Evidence is given that in some forms of secondary glaucoma (glaucoma in the Sturge-Weber syndrome, glaucoma secondary to uveitis) where the coefficient of outflow was in the normal range, the elevated intraocular pressure was due to increased aqueous formation.

In the two eyes in which the intraocular pressure was normalized by cyclodiathermy, there was no tonographic evidence of improved aqueous outflow, but a substantial drop in the net rate of aqueous formation was observed.—*Author's abstract.*

40. *Clinical Studies on Glaucoma (Klinische Studien zum Glaucomproblem).* HANS GOLDMANN, Berne, Switzerland. Ophthalmologica. *125*:16–21, January 1953.

Three cases are reported in which glaucoma developed in an eye in which the Schlemm canal system was open, but other ways of drainage of the aqueous outflow had closed. In 2 of these cases a cyclodialysis had been done previously; but when the cyclodialysis opening closed or partially closed, in 1 case following a cataract operation, glaucoma developed. In these 2 cases the intraocular pressure

in this second attack of glaucoma was much higher than that observed before the cyclodialysis operation. Gonioscopy showed the angle of the anterior chamber to be open at the time the attack of glaucoma developed. It would seem that in these cases the new routes of outflow established, which have a lower resistance than the Schlemm system, in some way interfere with the function of Schlemm's canal or tend to obliterate it; probably continuous function is essential for maintaining any route of outflow, including Schlemm's canal. 7 references.

ORBIT

41. *Carcinoma of the Orbit and Adnexa.* WILLIAM L. BENEDICT, Rochester, Minn. Tr. Am. Ophth. Soc. 1952.

Carcinomas of the orbit arise from four sources: the adnexa, the paranasal sinuses, distant organs by metastasis through the blood stream, and tissues within the orbit.

The greatest number of orbital carcinomas arise in the adnexa; from the conjunction of the skin and the conjunctiva on the lid margins, at the caruncle, and in the glands situated along the lid margins. Both squamous and basal cell-type carcinoma and probably adenocarcinoma arise at the corneal limbus. Basal-cell carcinoma (rodent ulcer) is the most common of the malignant lesions of the eyelids. Squamous cell lesions arise from the skin of the temporal region, the cheek and nose.

Epithelioma of the orbit and adnexa in 679 patients was recorded in the Mayo Clinic before 1950. The origins and extension are shown in the following table:

Upper lid		60
Lower lid		177
Limbus		31
Inner canthus		174
Orbital invasion from skin of nose, cheek, lids	102	
Upper lid	7	
Canthus and lower lid	27	
Sinuses	61	
Metastatic to orbit	4	201
Orbit primary		
Adenocarcinoma of lacrimal gland	17	
Mixed tumors	19	36
Total		679

Primary carcinoma of the orbit is rare, occurring most frequently as an adenocarcinoma of the lacrimal gland. Many of these are classified as "mixed tumors." Tumors that lie in the lacrimal fossa are not distinguishable as arising from the lacrimal gland except on microscopic examination, and even then there is uncertainty in some cases. Cylindromas are found in salivary and in lacrimal glands, but they also frequently form an element of the mixed tumors. Within the orbit, they are encapsulated, easily movable, and easily removed by blunt dissection. At first, they exhibit slow growth. The fact that mixed tumors and cylindromas may be encapsulated and not fixed to bone makes possible their complete removal without enucleation of the eye or exenteration of the orbit.

Metastatic carcinoma of the orbit is an extremely rare tumor. Adenocarcinoma of the breast, gastrointestinal tract, and the genitourinary tract spreads through the blood stream. Early surgical removal of epitheliomas with extensive excision of surrounding tissue is advocated to avoid recurrence and the necessity for radical exenteration of the orbit. A review of the cases reported in this series points strongly toward adoption of a more drastic policy in the early management of carcinoma of the adnexa. Irradiation is so uncertain that one cannot conscientiously depend upon it.—*Author's abstract.*

ANESTHESIA

42. *Akinsia of the Orbicularis.* WALTER S. ATKINSON, Watertown, N. Y. Abstract of paper read at Post Testimonial Program, St. Louis, March, 1953.

A different site is advocated for the injection to produce a block of the facial nerve and temporary paralysis of the orbicularis muscle. It is along the inferior edge of the zygomatic bone upward and across the zygomatic arch—it is given close to the bone. The index finger of the other hand is placed over the arch of the zygoma just anterior to the ear over the facial artery and vein. This is done to protect the facial vessels from being pierced by the needle and to indicate the direction the needle should follow and where it should stop.

This site is preferred because the landmarks are easy to find, ballooning of the lids does not occur, the lower branches of the facial nerve that supply the lips and lower muscles of the face are seldom blocked, postoperative pain on moving the jaw does not occur, only 3–4 cc. of the anesthetic solution is required, failure to secure a complete block is rare, and the injection is simple and easy to make.—*Author's abstract.*

MEDICAL OPHTHALMOLOGY

43. *New Air Force Visual and Ophthalmological Requirements.* EARL MAXWELL, Washington, D. C. Amer. J. Ophth. *36*:353–56, March 1953.

An explanation is given of a new regulation of the United States Air Force covering the eye requirements for all types of flying and nonflying physical examinations. Conditions causing nonacceptability for enlistment, commission, and for the various classes of flying are outlined. A consolidated chart of the eye requirements in all categories is inclosed.

For flying training as pilot (Class I) visual requirements are at least 20/20 for distant and near with a refractive error of not more than +1.75 or —0.25 with astigmatism of not more than 0.75. The maximum allowance in the phorias are Eso 10, Exo 5, Hyper 1. The point of convergence needs to be 70 or less. The accommodation must be at least the minimum for age as shown in Duane's chart. The color vision must be normal in that they must make four or fewer errors on the 17 plate test. Depth perception must be normal on a Verhoeff, or 30 or less on the Howard-Dolman apparatus, or no errors on the Armed Forces Vision

Tester. With visual fields 15° loss in any meridian disqualifies, as does scotoma. Night vision testing is not required unless the history shows evidence of defective night vision. If this is true, a satisfactory score on the School of Aviation Medicine Tester is required. With the red lens test no diplopia within 20° of center of screen in the cardinal directions of gaze is permitted. Similar requirements are expressed in the article for observer training for flying, for control tower operators, radar operators, for commission in the U. S. Air Force, and for enlistment in the U. S. Air Force.

COMPARATIVE OPHTHALMOLOGY

44. *Otrivin in Ophthalmology.* PAUL HURWITZ, Chicago, Ill. Eye, Ear, Nose & Throat Monthly. *32*:140, March 1953.

The topical effect of otrivin* solution in 0.05 per cent and 0.025 per cent strength was studied in the eyes of more than 100 patients. Included in this group were bacterial, vernal, and allergic conjunctivitis; phlyctenular and interstitial keratitis; ocular congestive states, and epiphora. The results indicate that otrivin is an excellent ocular surface vasoconstrictor and decongestant. Its major indications, ophthalmologically, are in (1) epiphora of congestive or inflammatory origin; (2) photophobia of various etiologies, and (3) ocular hyperemia, where decongestion is desirable.

Thirty cases are tabulated. Of 13 patients with epiphora, 8 were relieved with otrivin instillations; of 14 cases of photophobia, 13 were improved. Other symptoms, such as smarting, burning, itching, and foreign body sensation, were alleviated. Blanching of the conjunctival vessels begins immediately following instillations and lasts several hours.

45. *Antihistaminic Drugs in Dermatology.* JAMES J. BARROCK, Milwaukee, Wis. Wisconsin M. J. *52*:179–83, March 1953.

Antihistaminic drugs have been prescribed in innumerable cases of diseases that have an allergic as well as a nonallergic origin. These drugs reduce the manifestations of many cutaneous diseases. All the patients do not exhibit similar sensitivity reactions. The drugs in order of their effectiveness in the author's office were: chlor-trimeton maleate, pyribenzamine, benadryl, pyrrololazote, thepherin, histadyl, and neoantergan. Long acting antihistamines are perazil, diparalene, repeat action chlor-trimeton maleate, and phenergan. Antihistamines provide symptomatic not curative relief for allergic diseases, such as asthma, rhinitis, urticaria, and pruritis ani. Antihistamines for effectiveness must be given very early in acute urticaria to procure favorable results. In severe forms of acute urticaria, intravenous or intramuscular injections were more effective. Angioneurotic edema or giant urticaria is less susceptible to these drugs. Phenergan

* Otrivin is a member of the imidazoline series of chemical compounds and is a product of Ciba Pharmaceutical Products, Inc., Summit, New Jersey.

given orally produced marked relief to angioneurotic edema of the face especially about the orbital areas. Chlor-trimeton maleate, pyribenzamine, and benadryl also have given patients relief.

In localized neurodermatitis of the upper eyelids, relief was obtained with the topical applications of perazil cream. Warm compresses of boric acid solution are applied to the eyelids followed by the local applications of perazil cream. Within a short time, the itching subsides. This therapy is aided by the prescribing of repeat action chlor-trimeton maleate tablets, one tablet three times per day after meals and one tablet before retiring. The dosage is then reduced to one tablet in the morning and evening after relief is obtained. Benadryl, decapryn, and phenergan were prescribed for their sedative effect as well as for relief of itching. Side reactions are manifold especially in patients taking large doses. Reaction will occur in the first few days after administration of the drug. The most common of the side reactions are drowsiness, vertigo, headaches, anorexia, nausea, and vomiting. Cutaneous lesions and blood dyscrasias have been reported. Withdrawal of the drug is indicated where these side reactions occur. *Author's abstract.*

MISCELLANEOUS

46. *On the Comparative Use of Silver Nitrate and Penicillin in the Eyes of the Newborn.* H. MALLEK, P. SPOHN, AND J. MALLEK, Canad. Med. Assoc. Jour. *68*:117–19, February 1953.

On alternate months penicillin and silver nitrate were used in the eyes of all newborn infants. Penicillin ointment, 2,500 units per cc., in a water insoluble base, was instilled in the conjunctival sac of each eye three times a day for three days, beginning immediately after birth. In a second series of cases, penicillin, 100,000 units per cc., was instilled at one application immediately after birth. All the patients were observed during their stay in the hospital for evidence of redness in the eye, lacrimation, purulent discharge, or swelling of the lids. One month after birth, and two months post-partum, a questionnaire was sent to all the mothers.

During the study, none of the infants who had either penicillin or silver nitrate required treatment for ocular infection. A control group, which had been treated with an ointment containing a penicillin free base, showed cases of conjunctivitis. The children treated with silver nitrate developed an immediate chemical reaction. The children receiving many applications of penicillin showed signs of mild irritation of the eyes, which was probably due to manipulation of the eyes. The group of children receiving the large single application of penicillin did not show any signs of irritation. The questionnaire revealed that there were slightly fewer complaints from the mothers of the children receiving penicillin than from the mothers of the children receiving silver nitrate. 8 references.

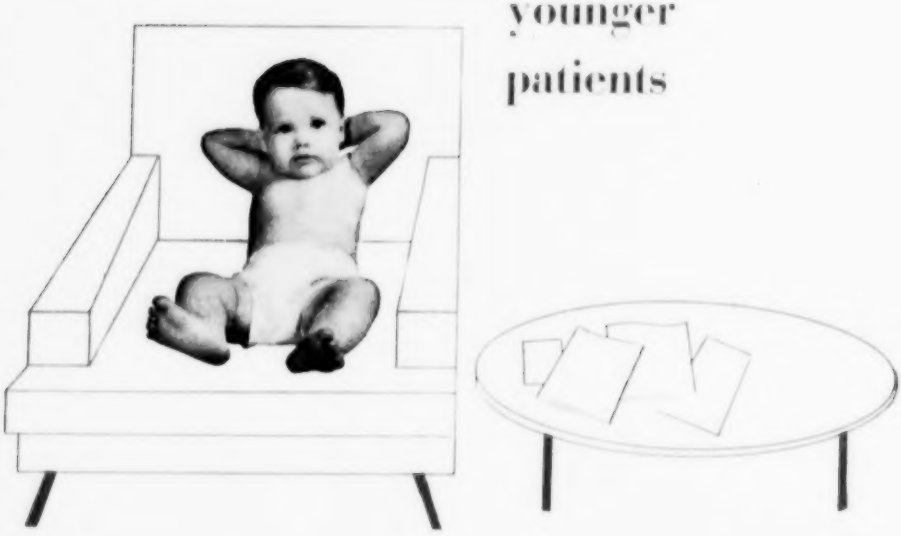
If you think of it tonight, just look around your own living room. You'll be amazed to note how many "arm's length" jobs there are! Yet many bifocal wearers are receiving only *two-thirds* of the help they need. Are they "really living?"

On the other hand, for presbyopes fitted with Univis Continuous Vision Lenses, the problem doesn't even exist. For the lady of the house who does the work in the living room, and for the breadwinner who relaxes there, visual requirements are met comfortably and naturally with Univis CVs, thanks to the prescribing doctor or dispenser. More than a million people enjoy comfortable, full-field vision with the lenses now known as CVs. The Univis CVs you prescribe are insured and guaranteed through your Univis laboratory.

univis THE UNIVIS LENS COMPANY • Dayton 1, Ohio

UNIVIS CVs FOR ALL PRESBYOPIC NEEDS

New for your younger patients



CRYSTALLINE

Terramycin

BRAND OF OXYTETRACYCLINE AMPHOTERIC

FOR WELL-TOLERATED, PROMPTLY EFFECTIVE BROAD-SPECTRUM THERAPY

PEDIATRIC DROPS

1.0 GRAM

new economy in drop dosage treatment

Each bottle of Terramycin Pediatric Drops supplies 1.0 gram of Terramycin, often a sufficient total dose for therapy of many common illnesses.

delicious raspberry flavor

The same good taste which makes Terramycin Oral Suspension a favorite for older children and adults on broad-spectrum therapy.

new flexibility in infant dosage schedules

Nonalcoholic Terramycin Pediatric Drops supplies 100 mg. of pure crystalline Terramycin amphoteric in each cc. to meet most infant dosage requirements; may be diluted as required.

SUPPLIED:

10 cc. bottles containing 1.0 Gm. crystalline Terramycin amphoteric in raspberry-flavored, nonalcoholic vehicle with specially calibrated dropper.

Pfizer

world's largest producer of antibiotics

CHAS. PFIZER & CO., INC., Brooklyn 6, N. Y.